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SCLEROMA

KLEBSIELLA RHINOSCLEROMATIS AND ITS EFFECT ON MICE

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AND

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IOWA CITY, IA.

A native-born resident of Iowa was recently seen at the University Hospitals with florid scleroma.[40] From this patient we recovered an organism satisfying the descriptions of *Klebsiella rhinoscleromatis* (see Table I). In reviewing the literature regarding this disease, rare in this area, we were puzzled by the contradictory statements regarding the etiological role of this organism in scleroma.

KOCH'S POSTULATES

Developing unequivocable proof of the etiological relationship between a specific micro-organism and a disease is very different from suspecting or having some evidence of a relationship. Koch first offered this kind of proof in a logical chain of experimental evidence, usually known as Koch's postulates. Briefly stated, these postulates are:

From the State University of Iowa and University Hospitals, Iowa City.

Supported in part by a grant from the Iowa Tuberculosis and Health Association and in part by a grant from the College of Medicine Trust Fund.

Submitted in partial fulfillment of the requirements for the degree of Master of Science in Otolaryngology and Maxillofacial Surgery.

1. The organism must be found in association with the disease.

2. The organism must be cultured outside the body of the host in pure culture for several generations.

3. Inoculation of a susceptible animal with a pure culture must reproduce the disease process.

4. The micro-organism must be recovered from the experimental infection in pure culture and shown to be the same as that inoculated.

For several important pathogens (e.g. *Treponema pallidum* and *Mycobacterium leprae*) their etiological roles have never been satisfactorily proved by Koch's postulates.

With *Klebsiella rhinoscleromatis* the controversy has centered about the third postulate, although fulfillment of some of the other postulates has been doubted or denied.[33,36]

Using the organism satisfying the currently accepted descriptions of *K. rhinoscleromatis* isolated from our patient, we carried out inoculation studies in white mice in the hopes of shedding some light on this subject.

HISTORY

Von Hebra, the Viennese dermatologist, published the first clinical description of scleroma in 1870.[44] He thought that it represented an atypical form of cutaneous cancer. Since then many causes of this clinical entity have been proposed, investigated, and debated in a voluminous literature which is still growing.

Few authors, whether presenting case reports or basic investigations, have failed to comment on the etiology. The various agents proposed include 1) a specific bacterium, particularly *Klebsiella rhinoscleromatis*, 2) synergism between two or more bacteria, 3) a specific virus, 4) synergism between a bacterium and a virus, including bacteriophage, and 5) an antibody-antigen reaction involving unknown antigens. None of these proposals is of recent mint; all were proposed and investigated before 1932 with excellent summaries in the reports of Belinoff,[2,3] Burack[4] and the Second International Otolaryngology Congress in Madrid (1932).[3] The digest of the reports of the Second International Otolaryngology Congress in English[36] suffered in translation and editing and lacks a bibliography.

In 1882 von Frisch[43] reported consistent recovery of a Gram-negative encapsulated rod from patients affected with scleroma. He attempted to produce lesions in animals by inoculation of this organism to fulfill Koch's postulates. He reported that small nodules at the site of injection in the nasal mucous membranes of mice showed some of the histologic features of human scleroma. A few investigators later reported typical scleroma lesions at the site of injection,[21,22,34,41] or a generalized septicemia and inflammatory process in the respiratory tract.[37] Other workers[31,36] were unable to confirm these results. Schroetter[34,35] was unable to reproduce scleromatous lesions in volunteers by implantation of scleroma tissue in the subcutaneous tissue of the forearm nor was de Simoni[6] able to produce lesions by installing into the nose packs soaked in the nasal secretions of scleroma patients.

The majority of articles on scleroma in English since 1932 have been clinical reports. Their comments on etiology, especially the relationship of *Klebsiella rhinoscleromatis* to this disease, often seem to be influenced by whether an organism fulfilling the descriptions of *K. rhinoscleromatis* (Frisch bacillus) was recovered. The contradictory reports of earlier investigators regarding fulfillment of Koch's third postulate in animal experiments apparently discouraged that form of investigation.

In contrast to the doubts about *K. rhinoscleromatis* in the western literature are the reports of Russian authors who seem to have accepted this organism as the etiologic agent of scleroma. They[26] report typical lesions in animals by inoculation. These studies are occasionally included in reports on the therapeutic use of vaccine produced by animal inoculations with *K. rhinoscleromatis*.

BACTERIOLOGICAL PROBLEMS

With the general use of antibiotics, the value of streptomycin, tetracyclines and chloromycetin in the treatment of scleroma soon became evident. These agents were found to be effective against *K. rhinoscleromatis* in in-vitro studies.[5,12,16] The reports of dramatic clinical response to these antibiotics, correlated with disappearance of *K. rhinoscleromatis* from the tissue and respiratory passages, argue strongly for the etiologic role of this bacterium.

A major stumbling block in the acceptance of *K. rhinoscleromatis* (or Frisch bacillus of the older literature) as the, or one of the, etiologic agents of scleroma has been the positive identification of this organism. Taxonomical classifications were created to serve as useful

concepts and are not absolute, all-inclusive classifications of organisms. The classification of Gram-negative rods has been difficult, derived slowly after much work by many bacteriologists, and even today it is only partially complete.

Several schemes of classifying the Gram-negative rods have been devised, but none is completely satisfactory. As newer biochemical tests were developed and applied to enlarging collections of Klebsiella-Aerobacter strains, increasing numbers of strains were found to be intermediate in their classification by biochemical methods. Variations were also noted in results obtained in the same test when performed by different investigators using slightly different criteria.

Progress was delayed until antigen analysis was applied. The capsular (K) and somatic antigens (O&R) have long been known but not until 1949 did Kauffman[20] clearly set forth the antigen and cultural forms of the Klebsiella.

I. Smooth Forms

   a. MKO forms—mucoid, capsulated with O antigen

   b. KO form—nonmucoid, capsulated with O antigen

   c. MO form—mucoid, noncapsulated with O antigen

   d. O form—nonmucoid, nonencapsulated with O antigen

II. Rough Forms

   a. MKR form—mucoid, capsulated without O antigen

   b. KR form—nonmucoid, capsulated without O antigen

   c. MR form—mucoid, noncapsulated without O antigen

   d. R form—nonmucoid, noncapsulated without O antigen

Since Kauffman set forth this scheme in 1939, Edwards and Fife[8,9] and others have found that the M antigen (bacterial slime of Kauffman) and K antigen (capsule) were serologically related and apparently identical. The O (somatic) and K (capsular) antigens are of interest in serological typing. At present 72 K antigens and 5 O antigens[9] have been described. Capsulated forms (MKO, KO, MKR and KR) are not acted upon by the O and R agglutinins, while the nonencapsulated forms (MO, O, MR and R) are agglutininated by their corresponding somatic antigens. Capsular typing of encapsu-

TABLE I: IDENTIFICATION OF KLEBSIELLA RHINOSCLEROMATIS

A = Acid only A&G = Acid & Gas A± = Acid only, slowly if at all V = Variable

	Typical Klebsiella pneumoniae (9, 12, 19, 46)	Klebsiella rhinoscleromatis (9, 19, 46)	Case 2 (F.B.) organism	K. rhinoscl. Levine–Hoyt criteria (24)
Gram stain	Neg	Neg	Neg	Neg
Morphology	Rod	Rod	Rod	Rod
Capsule	+,-	+	+	+
Large, Mucoid, Coalescent Colonies	+	+	+	+
Aerobic	+	+	+	+
Motility	–	–	–	
Voges–Proskauer (Acetyl methyl carbinol)	+	–	–	
Methy Red	–	+	+	
Indole	–	–	–	–
Nitrate	+	+	+	+
Citrate	+	–	–	
Urea	+	–	–	
Glucose	A&G	A	A	A
Lactose	A&G	–	–	–
Maltose	A&G	A	A	A
Mannite	A&G	A	A	A
Sucrose	A&G	A	–	A±
Xylose	A&G	A	A	
Salicin	+	+	+	
Inositol	+	+	+	
Adonitol	+	+	+	
Dulcitol	V	–		
d-Tartrate	+	–	–	
H_2S	–	–	–	
Gelatin	–	–	–	
Mucate		–	–	
O Antigen	1–5	2 (2A)	2	
K Antigen	1–72	3	3	

lated forms can be accomplished relatively easily by a variety of techniques using specific capsular typing sera.

Kauffman[19] applied the name *Enterobacteriaceae* to a large family of Gram-negative, non-sporing rods, which are either motile with peritrichous flagellae or non-motile. They grow on ordinary media, ferment glucose with or without gas formation, and reduce nitrates to nitrites.

By means of biochemical characteristics he divides the family Enterobacteriaceae into tribes and generae and species. Most of these species are further classified by serological tests into seriological subgroups and types.

In this scheme the genus *Klebsiella* includes a large group of related Gram-negative, non-sporing, non-motile rods, usually encap-

sulated and usually producing mucus but not indole. They split adonitol and inositol, often do not decompose urea, give a positive Voges-Proskauer reaction, but a negative methyl red test. They usually grow on an ammonium citrate medium and ferment lactose.

Kauffman[19] recognized only two species of Klebsiella: *K. rhinoscleromatis* and *K. pneumoniae*. They are distinguished on biochemical grounds. This view was accepted by Edwards.[9]

In Table I are listed the typical biochemical reactions of these two species and the reactions of the organism isolated from a patient suffering from scleroma reported by one of us[40] elsewhere. This organism was used in the experiments described below.

In this scheme *Klebsiella rhinoscleromatis* has an antigen formula of O group 2 (specifically 2A, Kauffman) and K group 3 (Group C, Julianella).[19] The reports of the biochemical activity of organisms with this antigenic formula have been remarkable in their agreement, considering the wide biochemical variation found with other Klebsiella strains. Determining that a strain of Klebsiella with the biochemical characteristics ascribed to *K. rhinoscleromatis* has the antigen formula O2:K3 lends considerable weight to the identification.

Capsular K antigen 3 was found by Kauffman to occur with Klebsiella belonging to both O group 1 and 2. For this reason descriptions of Klebsiella possessing a type 3 K (capsular) antigen and displaying biochemical activity differing from the reactions ascribed to *K. rhinoscleromatis* (e.g. the aerogenic, dulcitol-positive strain used by Epstein[12]), should be suspected of possessing O antigens other than group 2. They should not be used as an argument against the speciation of Kauffman's scheme until their O antigens have been determined.

In contrast to the acceptance of Klebsiella capsular sero-typing in investigative and some clinical applications, determination of the somatic antigen (O) is rarely carried out because it is difficult. One method of ascertaining the O antigen can be illustrated by quoting Dr. Phillip Edwards' report[7] on the organism used in these experiments:

"We were able to isolate a capsule-free mutant from the culture by plating and examination of many colonies. This mutant was agglutininated by serum prepared from organisms belonging to O group 2, but not sera derived from members of O groups 1 and 3. These

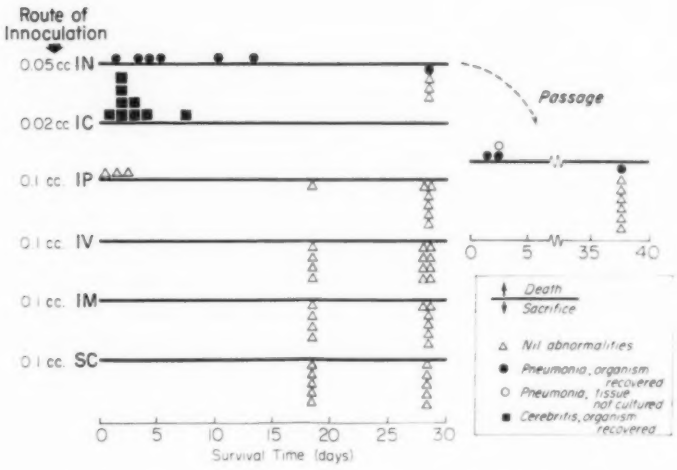


Fig. 1.—*Routes of Inoculation*—20-day-old albino male mice inoculated with a 16 hr (37°) brain-heart infusion culture of *Klebsiella* rhinoscleromatis (recovered from a patient with scleroma) titrated to contain 10^8 organisms per cc. Dosage indicated with route. Passage of organism recovered in pure culture from the lung of a mouse dying fourteenth day after intranasal inoculation with pneumonia. IN, intranasal; IC, intracranial; IP, intraperitoneal; IV, intravenous; IM, intramuscular; SC, subcutaneous.

sera primarily were capsular sera prepared from organisms of other capsule types."

INOCULATION STUDIES

The question whether the inoculation of the Frisch bacillus into experimental animal will produce scleroma-like lesions has persisted throughout the years. Now that the problem of distinguishing related members of the Klebsiella-Aerobacter group has been partially solved, it seemed likely that the divergence of results could be explained on bacteriological differences. We, therefore, felt it worthwhile to undertake inoculation studies using our organism.

A. *Materials and Methods.* Twenty-day-old albino male mice of the C.F.W. strain were inoculated in groups of ten either intravenously, intraperitoneally, intranasally, intramuscularly, subcutaneously or intracranially, with a brain-heart infusion broth culture of

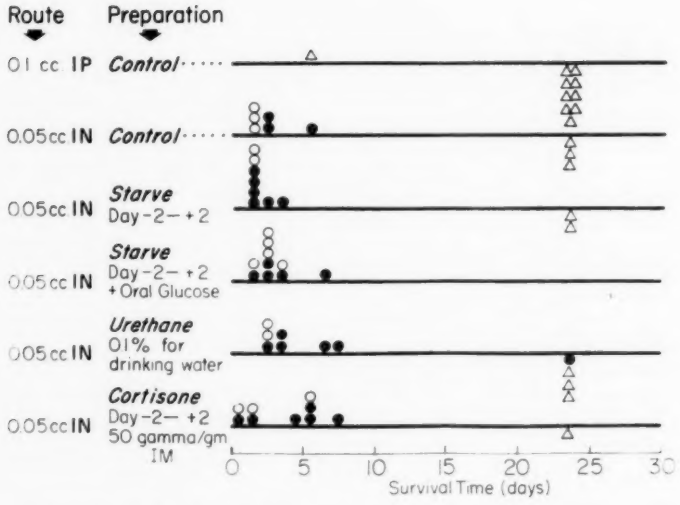


Fig. 2.—*Reduced Host Resistance*—Eighteen-day-old albino mice, prepared by various methods known to affect host resistance, were inoculated intranasally with a fourteen hour (37°) brain-heart infusion broth culture titrated to contain 10^7 organisms per cc. Intraperitoneally and intranasally inoculated mice, otherwise unprepared, were used as controls. Culturing of lungs of mice showing macroscopic pneumonia at death or when killed resulted in recovery of *K. rhinoscleromatis* in pure culture biochemically identical to the inoculated organism in every instance where culture was attempted. (See Figure 1 for explanation of symbols.)

K. rhinoscleromatis incubated at 37° for 16 hours. This organism had been subcultured four times in pure culture after recovery from a patient with scleroma. Titration of the inoculum revealed it to contain 10^8 organisms per cc. The amount administered by the various routes is shown in Figure 1.

B. *Results.* No deaths resulted from intramuscular, subcutaneous or intravaneous inoculation before these animals were killed on the nineteenth and thirty-first days after inoculation. All of the mice inoculated intracranially died of cerebritis. The intranasally inoculated mice developed extensive pneumonia. All mice were autopsied at death or when killed on the nineteenth and thirty-first days. Significant gross and microscopic findings were limited to the brain in the intracranially inoculated mice and the lungs of the intranasally inoculated mice. K. rhinoscleromatis was recovered in pure culture

from the brains of the intracranially inoculated mice and from the ground lungs of the intranasally inoculated mice. This pneumonia was peculiar in its chronicity and in the fact that large macrophages containing bacteria were present. These cells resembled the Mikulicz cells of human scleroma (Fig. 6). These cells became more prominent in the exudate as the period between inoculation and death or killing lengthened. Extensive pneumonia from which the organism was recovered in pure culture was found in a mouse killed thirty-one days after inoculation.

C. *Passage.* Organisms isolated from the lungs of a mouse dying on the fourteenth day in the first experiment were re-identified as K. rhinoscleromatis and re-inoculated intranasally into another ten mice in a measured dose, with the same results. All animals were autopsied at death or when killed on the thirty-third day. Gross and microscopic lesions observed were limited to the lungs. These results are shown in Figure 1.

D. *Effect of Reduced Host Resistance.* Mice were treated with various measures thought to reduce host resistance before and immediately following intranasal inoculation. These methods included: a) starving for 48 hours; b) starving for 48 hours and substituting 5% glucose for the drinking water; c) Cortisone® 50 gamma/gram/day IM from two days before to two days after inoculation; and d) substituting 0.1% Urethane® for the drinking water from two days before to two days after inoculation. Controls were unprepared mice inoculated intranasally or intraperitoneally with the same inoculum. The resulting mortality is shown in Figure 2. K. rhinoscleromatis was recovered from the resulting pneumonia in pure culture from the lungs of mice with macroscopic pneumonia at autopsy in all cases where an attempt was made to recover the organism.

E. *Macroscopic Pathology.* The lungs of mice dying on the first and second days were extensively involved in a lobar and focal manner and exhibited a liver-like consistency on cut-section. The pleural surface of involved portions was of a uniform dark red color. Mice dying on the third day had more focal lesions; the pleural surface of completely involved portions had yellow-brown spots on a dark red background alternating with normal collapsed white lung, if the whole lobe was not involved. Mice surviving longer showed more patchy but extensive pneumonia, with foci of varying age (Fig. 3).

A mouse killed on the thirty-first day after inoculation was found to have extensive involvement of three lobes (not unilateral). The pleural surface of the affected portions was greyish-brown in

Fig. 3.—*Pneumonia in Mouse*—Gross appearance of lungs of mouse killed six days after intranasal inoculation with *K. rhinoscleromatis*. Diseased lungs on the left; normal lungs for comparison on the right. The normal lungs are collapsed and uniform in color and outline. The diseased lungs show the irregular outlines of inflammatory foci of different ages. These vary from yellow to red-brown in color and in size from minute dots to involvement of a whole lobe.

color and irregular. Areas varying from dark brown to grey-white were seen on cross-section. These changes were present also in the lungs of a mouse killed thirty-eight days following inoculation.

F. *Histologic Pathology*. Lungs of the mice dying on the first day of the intranasal inoculation showed massive distention of the alveolar capillaries, large and small vessels and some escape of red blood cells into alveoli. Trabecular collapse had occurred over large areas. Only slight periarterial edema was present. Inflammatory cells, and bacteria were rare. The bronchial tree was free of exudate.

In mice dying on the third day the process was more focal. Vascular changes seen in mice dying on day 1 and day 2 were prominent in some areas. Other areas had an older process with alveoli distended by an exudate containing degenerating polymorphic neutrophiles and

a moderate number of macrophages and plasma cells. Innumerable bacteria were present, both free in the alveoli and within macrophages. The swollen vascular adventitial spaces contained many bacteria. These foci appear to be centered around arteries, the older portions nearer the vessel and less intense and newer changes at the periphery (Fig. 4b).

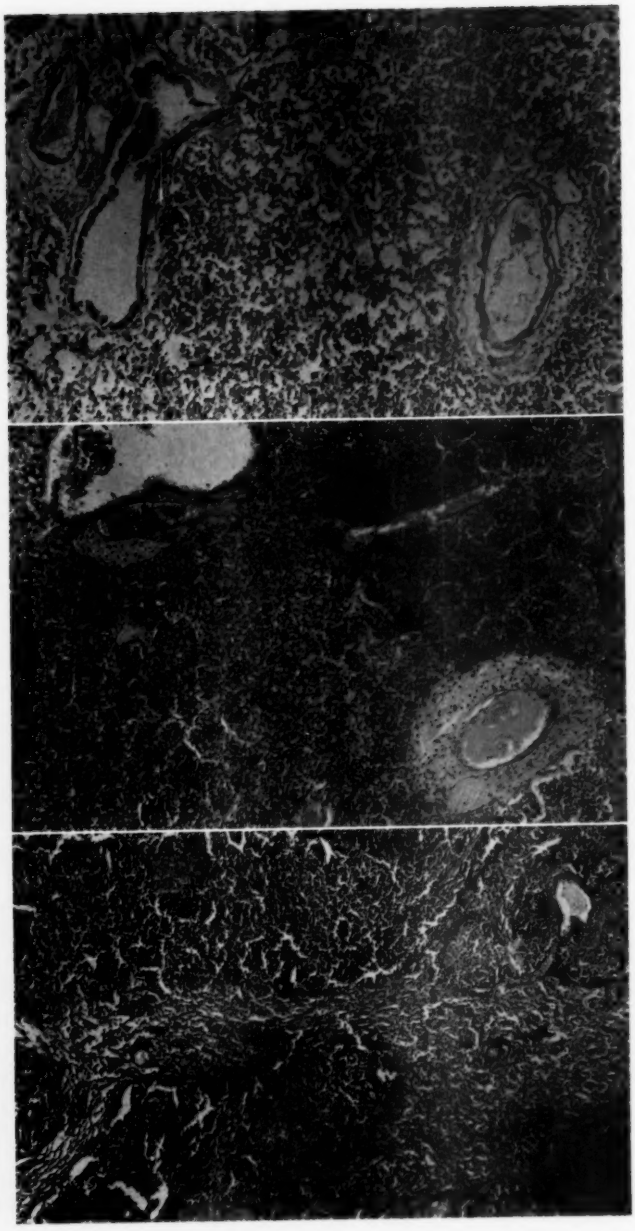
Survivors to the fourth, fifth, and sixth days had even more focal distribution of lesions, but extensive involvement of three or more lobes. In addition, plasma cells and macrophages were the predominate cells in the exudate, filling large areas of alveoli and periarterial spaces. Many bronchi were plugged with debris; however, the bronchial mucosa was preserved. Large swollen cells containing bacteria were prominent. These changes were also seen in a mouse dying on the eleventh day after inoculation.

The lung of a mouse killed on the twenty-fourth day showed a consolidative process chiefly centered around the vessels, with a dense plasma cell infiltrate containing large cells with lacy and almost clear cytoplasm (with H&E stain) containing bacteria. The vessels in the involved areas showed hyalinization and the bronchi were plugged with debris.

Thirty-one days after intranasal inoculation a mouse was killed and found to have consolidation of three lobes into a firm greyish-brown mass. K. rhinoscleromatis was recovered from the ground tissue in pure culture. Histologically this tissue was composed of focal perivascular, peribronchial repair processes containing many plasma cells and large macrophages. No significant necrosis was found. A mouse killed at thirty-eight days demonstrated the same perivascular repair process. K. rhinoscleromatis was recovered from the ground tissue of all these late lesions in pure culture (Figs. 4c, 5).

G. *Comparison to Human Scleroma.* Certain features of the histopathology of these late lesions are similar to that found in human scleroma. In essence both scleroma and this pneumonia could be characterized as chronic granulomatous inflammations without necrosis or tubercle formation. Large cells containing bacteria with lacy cytoplasm was found regularly, as well as a predominately plasma cell exudate with Russell bodies. Hyalinization of vessels was also prominent.

H. *Viral Studies.* Our investigation of a possible primary viral or symbiotic viral agent was limited to egg inoculations with biopsy



tissue obtained from the patient. A virus was not recovered. We hope to investigate this possibility with tissue-culture techniques if we find another patient.*

COMMENT

Of the various routes of inoculation studied, only the intracranial and intranasal routes consistently produced lesions. Inoculation by other routes failed to produce gross or microscopic changes, either at the site of injection or systemically.

The effectiveness of the various methods studied which might reduce host resistance to this organism seemed to be greatest with the starvation and starvation-plus-oral glucose techniques. This, in another study, has also been demonstrated for staphylococci.[39]

The prolonged course of the pneumonia produced by intranasal inoculation of mice with K. rhinoscleromatis parallels the course of scleroma in humans as an extremely chronic granuloma.

Mice have long been known to contract pneumonia experimentally from a wide variety of human bacterial, ricketsial and viral pathogens. References to the pertinent literature are included in a recent article by Epstein[13] describing an intraoral method of inoculation. His method appears to have advantages of better quantitation and less contamination than the intranasal method under ether anesthesia used in our experiments.

In 1959 Epstein and Payne[10] published a study of the virulence of selected strains of Klebsiella for mice using the oral and intraperitoneal routes. Their strain 5048 (strain 5049 is its noncapsulated mutant) possessed a type 3 capsule. From Epstein's other writings[12]

* Our virus and serological studies were conducted by Dr. Albert McKee in the Department of Bacteriology.

Fig. 4.—*Pneumonia in mice after intranasal inoculation with K. rhinoscleromatis*: a) *Two days after inoculation.* Large areas of alveoli containing acute inflammatory cells; some edema of the perivascular spaces. H&E x75. b) *Three days after inoculation.* Huge ballooning of the perivascular adventitia. The alveoli are filled with neutrophiles, cellular debris, plasma cells, macrophages and bacteria. The bronchus is almost free of exudate and its mucosa is preserved. H&E x75. c) *38 days after inoculation.* Alveolar outlines can no longer be recognized in this dense granulomatous process. No areas of necrosis were found. H&E x75. See Figure 5. pure culture from the ground tissue of this lung. H&E x300.

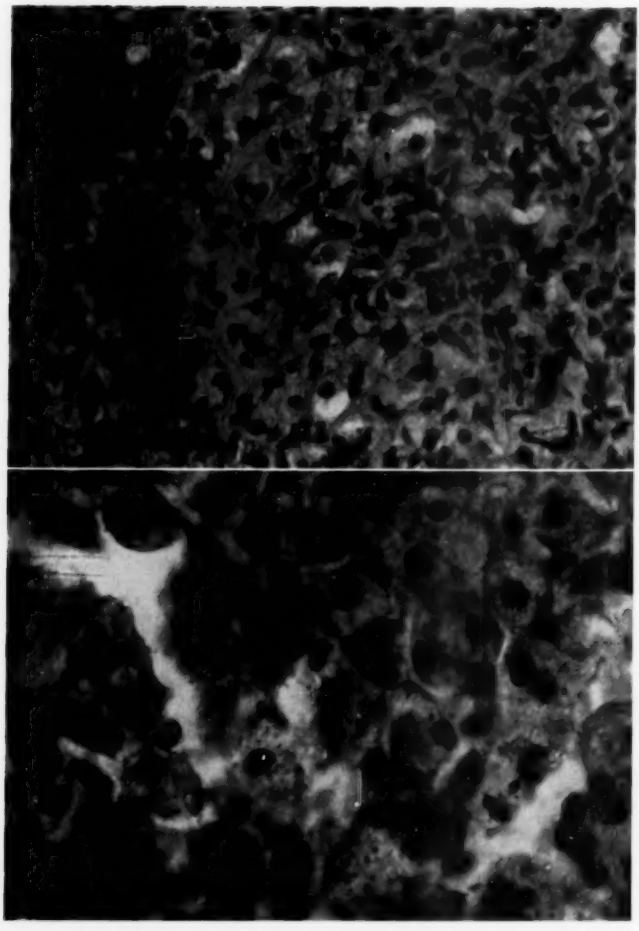


Fig. 5.—*Pneumonia in Mouse 38 days after Intranasal Inoculation with K. rhinoscleromatis.*—Alveolar outlines in this area have been lost and replaced by a granulomatous repair process in which Mikulicz-like cells, plasma cells and Russell bodies are common. *K. rhinoscleromatis* was recovered in pure culture from the ground tissue of the lung. H&E x300.

Fig. 6.—*Macrophages Containing Bacteria as part of an Extensive Pneumonitis in a Mouse killed 24 days after Intranasal Inoculation with K. rhinoscleromatis.*—They resemble the Mikulicz cells of human Scleroma. *K. rhinoscleromatis* recovered in pure culture from the ground tissue of this lung. H&E x850. Fluorite objective.

it appears to possess biochemical properties of *K. rhinoscleromatis*. These investigators found marked differences between the virulence of different Klebsiella strains and the effect of varying the route was not the same in all cases. Some strains were highly virulent by the oral route, some less so, and others appeared to be avirulent. Two strains were more virulent by the intraperitoneal route. They found strain 5048 to be of low virulence by the oral route and virtually avirulent in both the capsulated and noncapsulated form by the intraperitoneal route. Orally the capsulated variant was 100 times more virulent than the acapsular strains.

Their findings of low virulence or avirulence of this strain by intraperitoneal route and long survival time with pneumonia when inoculated through the upper respiratory passages were confirmed in our studies. The strain used in our experiments, however, not only possessed the biochemical and serological characteristics of *K. rhinoscleromatis* but also had been isolated from a patient with the clinical and histopathological features of scleroma.[10]

The histology of experimental pneumonia in mice produced by various bacterial agents is said to be similar. The essential features are well described and illustrated in an article by Hoyle and Orr.[18] Epstein[11] studied the histopathology of the acute phases of experimental Klebsiella in mice with particular references to the dilatation of the periarterial adventitial spaces.

In the acute phases the histology of the pneumonitis produced by intranasal inoculation with our strain of *K. rhinoscleromatis* was similar to that described with other bacterial agents. As the time lengthened between inoculation and death, however, a chronic granulomatous process supervened in which macrophages, plasma cell exudate and fibroblastic activity were prominent. Necrosis and giant cells were not found. The normal lung architecture in these late lesions could no longer be recognized, having been replaced by the granuloma.

These changes and the presence of large macrophages with lacy cytoplasm in which bacteria could be seen are a striking parallel to the histology of scleroma in humans.

Since *K. rhinoscleromatis* was invariably recovered in pure culture from the involved tissue and the disease process was reproducible by passage after several subcultures, there can be little doubt that the lesions produced were the effects of the host-parasite relationship between mice and *K. rhinoscleromatis*.

SUMMARY

Scleroma, a chronic granulomatous affliction of the upper respiratory tract, has been attributed to various etiologic agents, particularly a specific bacterium, *Klebsiella rhinoscleromatis*. *K. rhinoscleromatis* has not been universally accepted, and the reported results of inoculation studies are contradictory.

Using an organism satisfying the currently accepted criteria of *K. rhinoscleromatis* isolated from a patient with florid scleroma, mice were inoculated by various routes. Detectable pathology was produced only by intranasal and intracranial inoculation. The pneumonia produced by intranasal injection was a chronic granulomatous process with many of the features of human scleroma. Attempts to recover the organism from the experimentally produced infection in mouse lungs were invariably successful.

By these studies we believe Koch's postulates have tentatively been fulfilled and that *Klebsiella rhinoscleromatis* bears an etiological relationship to scleroma. Ultimate proof of the relationship, however, rests in the reproduction of the disease in humans.

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LXX

THE UPPER PHARYNX

A REVIEW

Part I, Embryology, Anatomy

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In air-breathing species, the pharynx conducts the streams of respiration and ingestion, and these streams are separated by valvular systems in the upper and the lower portions of the "aero-digestif" tract.[1] The laryngeal system has been reviewed recently by Pressman and Kelemen[2] and the pharynx in deglutition has been reviewed by Bosma.[3] Homologic variations in this region of the body have been comprehensively reviewed by Negus[4-11] and earlier by Nemai[12] and by Rückert.[1]

The mechanism by which respiration and ingestion are separated in the upper pharynx is basically similar in many vertebrates, but with heterogeneous adaptations. These adaptations differ among species and probably sequentially within species, such as the frog, which adapt to successive environmental situations. Change in the manner of feeding is another factor in progressive development of the pharynx. Thus, adaptation of the pharynx occurs as the human infant matures from suckle feeding to mastication and swallowing of food masses.

These patterns reflect general adaptation of the organisms to their environment, whether in air or water, and also specific adaptation to the manner of respiration and feeding. In some species, such as the reptilia and the herbivora, respiration may proceed almost continually, with the respiratory airstream penetrating the pharynx through a duct-like epiglottis extending from the larynx through an enclosing orifice in the palate. In others, the pharynx is a common chamber reciprocally utilized. Thus, in some of the amphibia, it is engaged

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either in glossopharyngeal respiration or in conducting food to the esophagus. In most mammals, the pharynx is alternatively concerned with swallow or with respiration, and in the human the palate participates with the tongue in formation of a retro-oral portal or barrier by which penetration of the bolus into the pharynx is controlled. The most extensive adaptation of the upper pharynx occurs in human postnatal development, with gradation from an arrangement comparable to that of higher mammals to the distinctively enlarged, stabilized, and mobile arrangement of the mature human pharynx. This extensive developmental modification of the upper pharynx is associated with physiologic maturation, by which the extraordinary motor achievements of human speech are accomplished without impairment of the basic action of swallowing and without obstruction of the route of unmodulated respiration. These anatomic and physiologic maturations are of increasing interest to the otolaryngologist, plastic surgeon, neurologist, speech pathologist, and orthodontist.*

EMBRYOLOGY

Orientation to embryogenesis of the pharyngeal region contributes to our understanding of the developmental and interspecies variation of its anatomic forms. The pharynx is basically a sleeve, or cylinder, extending from the basicranium to the esophagus. The upper pharynx is differentiated later in fetal development than the lower pharynx, is developmentally more complex, and continues its morphologic change for a longer period in fetal and postnatal life.[15] The most complex development, as well as the greatest interspecies variation, occurs in the ventral wall of the pharynx (Figs. 1 to 8). Here the embryonal foregut is penetrated independently and successively by the stomodeum and by the nasal cavities.[16] In the mam-

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* Terminology employed in this review:

Upper pharynx—The term is defined as the palate, its extensions and musculature, and the adjacent portion of pharynx. This regional term is employed as a more general reference, compared with *epipharynx*, which refers to the pharynx above the palate, or *mesopharynx*, which is that portion between the palate and epiglottis.[14] The palate and palatopharyngeal folds are referred to in combination as the *palatopharyngeal partition*.[3]

Spatial orientation within the organism is described in reference to the standard *sagittal*, *frontal*, and *transverse* anatomic planes. Directions of displacement in reference to the organism are in corresponding anatomic designations as *cephalic*, *caudal*, *ventral*, and *dorsal*. *Rostrally* or *rostrad* is used in reference to the ventral-cephalic terminus or tip of the organism. This term is particularly useful in describing lengthwise phenomena of the pharynges of the several species which do not lie strictly in the cephalo-caudad or longitudinal body axis. Upper or lower, anterior or posterior are occasionally used in description of mature upright human actions, to correspond somewhat with clinical literature.

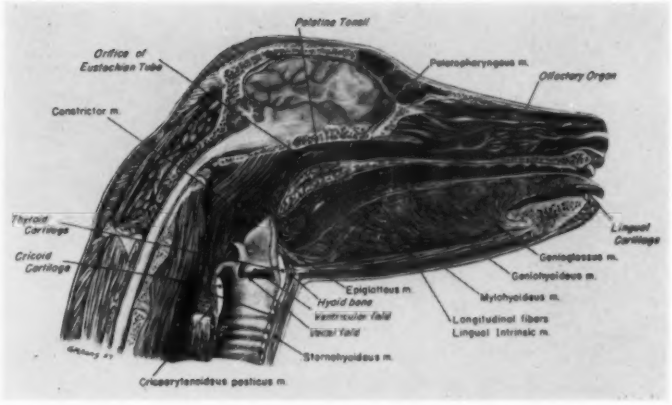

Fig. 1.—Sagittal view of head and neck of dog. Septum of nose excised to show olfactory organ.

malian embryo, the stromodeum and nasal cavities are initially confluent dorsal to the "primary palate."[17-19] Later this single cavity is demarcated into nasal and oral cavities by the converging processes of the "secondary palate" to form the hard palate and also the primordium of the soft palate.[20,21] The mobile or "soft" palate is thus derived at the site of convergence of nasal, oral, and pharyngeal cavities and extends secondarily into the pharynx.*[22]

The contours of the upper pharynx are determined by its adjacent skeleton early in fetal life.[32,33] Cephalically and dorsally it is in proximity to the basicranium and, with human postnatal enlargement and descent of the pharynx, its dorsal wall adjacent to the palate is in approximation to the first and second cervical vertebrae.[34] Ventrally,

* The mechanism of embryogenesis of the palate is indicated by the variety of deficiencies of its development. The most common of these is gross cleft of the soft palate, possibly with extension of the cleft into the hard palate, and with variable hypoplasia of the anomalous vanes of the hemipalate and palatopharyngeal folds. The varieties of hypoplasia without cleft or with cleft of only the uvula[23-28] are more subtle. These are commonly described as "short palates," though estimation of relative length of the palate by inspection through the mouth is notoriously difficult. A lateral roentgenogram may reliably demonstrate relative shortness, as well as a diminution in thickness. In appropriate coincidence with hypoplasia of the palate there may be a median notch of the hard palate at the junction with the soft palate, detectable by palpation or by roentgen palatography, or in older children by visualization incident to palatal elevation.[24,29-31] Selective deficiency of musculature in these circumstances of anomaly has received comparatively little attention.

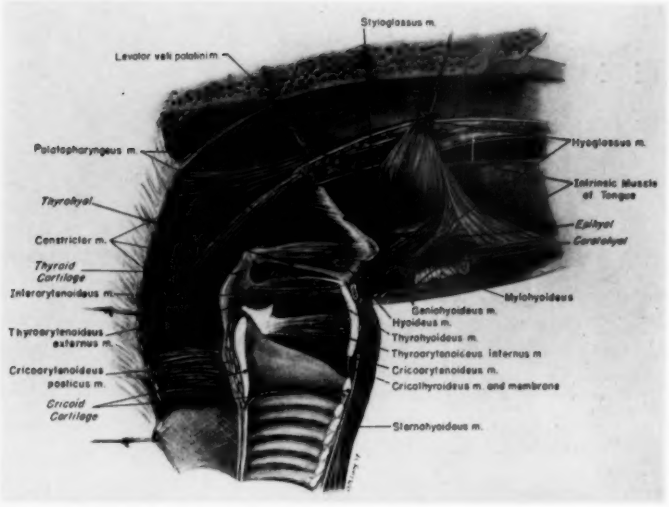

Fig. 2.—Dissection of dog from sagittal plane, showing intrinsic muscles of pharynx, tongue, and larynx. Hyoglossus is separated at origin and reflected to demonstrate musculature of tongue.

it is in continuity with the nasal cavities at the posterior choanae. An exceptional adaptation found in the rat is that of a pharyngeal canal prolonged into the center of the nasal cavity.[35] The upper pharynx is supported laterally by musculature extending from the eustachian tube and the styloid processes.[36]

Embryonic derivation of the *pharyngeal musculature* has been comprehensively studied by Edgeworth.[37] He concludes that "the primitive condition appears to have been an anterior constrictor—the stylopharyngeus, and a posterior constrictor. From the posterior constrictor was developed a longitudinal stratum—the palatopharyngeus." In some species, the stylopharyngeus derivatives are arranged to provide lateral traction upon the pharyngeal walls—to dilate the pharynx. This is an arrangement which would potentially give the pharynx a negative as well as a positive mechanical action.

In many mammalian forms, such as the cat, dog, and monkey,[38] the styloid musculture joins the articulated sections of the stylohyoid skeleton by which the pharynx is suspended and is moved in relation to the basicranium and the cervical structures. During swallowing

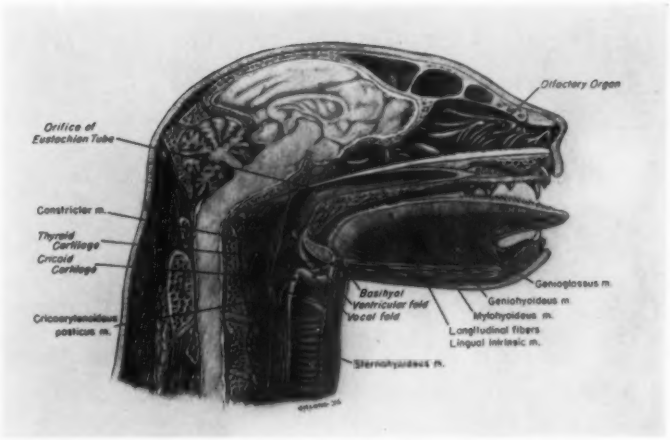

Fig. 3.—Sagittal view of head and neck of cat. Septum of nose excised to show olfactory organ. The head is relatively flexed at neck.

this styloid musculature contracts with the constrictor[39] to move the ventral portion of the pharynx as a whole cephalad while the organ itself is contracting. In the human, lacking a continuous stylohyoid skeleton, the styloid muscles probably also contract synergistically with the constrictors in swallow, to aid in accomplishment of the characteristic cephalad displacement of the pharynx and adjoining structures in that performance.

The superior constrictor is formed later in embryogenesis than the other constrictors and its cephalic portion is the most variant among different species.[3] In most primitive mammals a superior constrictor is absent.[37] As the animal scale is ascended, however, additional elements appear until the typical primate picture is attained.[40]

The differentiation of the pharyngeal musculature converging upon the palate well illustrates the basic principles of development in this area. The shelf-like palatopharyngeal folds are penetrated by embryonal mesoderm from the adjacent constrictor[21,22] in a manner similar to penetration of musculature into the tongue[22,41,42] or into the turbinates.[17] The palatopharyngeus is the prologue of the levator veli palatini and salpingopharyngeus, which are derived secondarily from its cephalic portion. This spatial orientation of the palatopharyngeal folds within the pharynx is subject to much interspecies

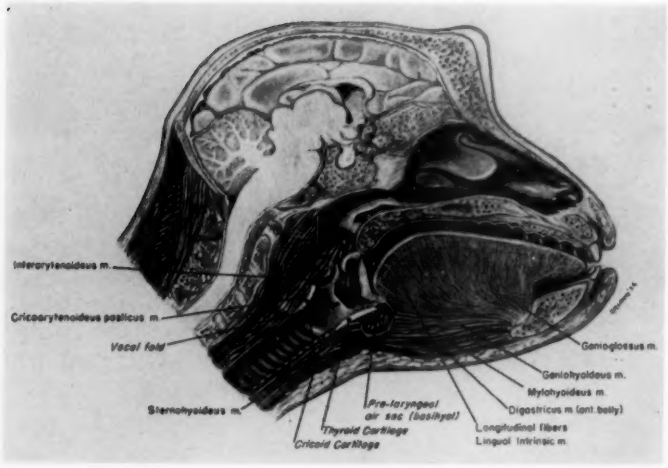

Fig. 4.—Sagittal view of head and neck of monkey.

variation, as described by Negus.[6] House[40] mentions that in the rat the palatopharyngeus muscle originates in the substance of the soft palate. Chaveau[43] describes a condition in the rat in which the pterygopharyngeus arising from the pterygoid process partially blends with the palatopharyngeus. In the rabbit,[37] the palatopharyngeal folds meet in a median dorsal fold at the junction of the pharynx and the esophagus. This longitudinal muscular system is most completely developed in the human.

The palatopharyngeus in the human is a broadly arching muscle which originates from the dorsal margin of the hard palate and on the dense connective tissue of the soft palate, to interweave and insert into the lateral and dorsal aspects of the pharynx in continuity from the level of the hard palate through the length of the mesopharynx and possibly the hypopharynx (Figs. 5 and 8). The cephalic margin of insertion of the palatopharyngeus upon the constrictor is distinct and the more constant.[44,45] Despite many attempts to anatomically distinguish the motor elements of the constrictor from those of the palatopharyngeus, this distinction is comparatively lacking.[45-52] Interdigitation of palatopharyngeal fibers at this level with fibers from the midportion of the superior constrictor[31,49,50,53,54] also led to argument as to functional designation. Thus, a difference of opinion exists as

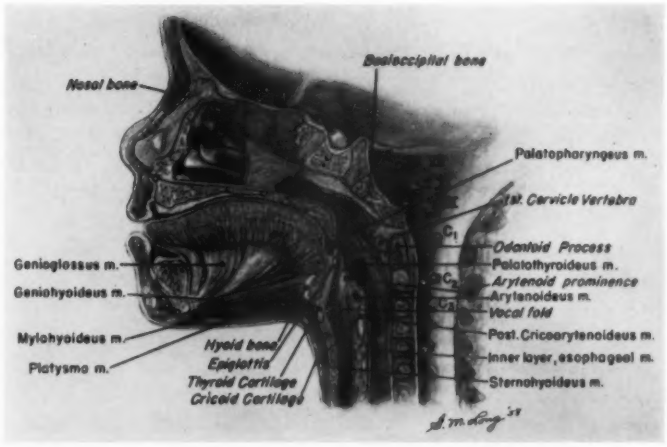

Fig. 5.—Saggital view of head and neck of human infant.

to whether the convergence of the pharynx about the palate represents action of the palatopharyngeus or of the constrictor. When we note that in the human and in a variety of subhuman species the palatopharyngeus originates at the dorsal and lateral walls of the pharynx and migrates toward the palate in close juxtaposition to the constrictor from which it originates, it can be seen that there is little point or profit to attempted embryologic, mechanical or nosologic distinctions of this sort.

The caudal extent of the palatopharyngeus insertion upon the pharyngeal wall is variable,[49] but a consistent anatomical arrangement is that of attachment of the most ventral portion of this fan-like muscle, as the "palatothyroideus" (Fig. 5), to the dorsal superior horn of the thyroid cartilage.* The palatopharyngeus is variable in general size in relation to the palatopharyngeal folds.[37,53]

The levator veli palatini is probably the most constant muscle of the upper pharynx in form and in termination.[36] The levator is distinguished by Rüdinger[55] into a portion inserting upon the hard

* This designation of palatothyroideus as the portion of the palatopharyngeus which inserts upon the thyroid cartilage is that employed on the basis of observation and historical review.[49] Oldfield and MacNaughton[52] designate as palatothyroideus a larger area of the lower portion of the palatopharyngeus than that inserting upon the thyroid.

palate and two portions inserting into the soft palate. This latter distinction is not readily discerned in dissections by the present writers. The salpingopharyngeus, however, is one of the most variable, consisting usually of shreds of muscle dispersed within the fascia of the salpingopharyngeal fold.[36]

The tensor veli palatini is of different origin than the other paired muscles mentioned above. It is related in development and position to the pterygoid structures[56,57] and, as indicated by its distinctive innervation via the trigeminal nerve, is derived from musculature of the mandibular arch rather than from the mesenchymal prologues of the other structures in the pharyngeal region.

* * *

The distinctive specializations of the upper pharynx are those of the flap-like palate which protrudes from the ventral pharyngeal wall and of the constrictor musculature, supplemented by a system of sphincters converging upon the palate. The homologic variations of the palate are closely related to those of the eustachian apparatus.[55,57-61]

A "soft" palate is absent in amphibia and in most reptiles.[6] In the birds, the palate is represented by a group of granulated papillae.[6,62] In the crocodile the hard palate extends to the dorsal portion of the pharynx and, as illustrated by Negus,[11] the posterior choanae are correspondingly dorsally displaced. The crocodile has a small soft palate, with a well-developed palatopharyngeal sphincter enclosing the tip of the epiglottis. The typical mammalian palatal arrangement as described by Wood-Jones[49] is that of a palatal plate with palatal folds aligned with it to form an oblique "palatopharyngeal partition"[63] within the pharynx, which acts as the dorsal wall of the food channel. This simplified arrangement was found by Townshend[50] in a 3-month human fetus. Oldfield and MacNaughton[52] described an adult in whom the palatopharyngeal folds converged to form a posterior diaphragm ventral to their insertion into the pharyngeal wall, thus constituting a structure much like the palate of certain lower mammalian species.[37,46,49] A patient having this pattern of anomaly has also been studied by one of the writers (J.B.). Similar abnormalities of form may be found in cicatricial stenosis of the upper pharynx following surgery or inflammatory disease.[64] An opposite variation is that of absence of the palatopharyngeal folds as described in monotremes by Göppert.[65]

In its basic or simplest form, the palate is apparently capable of little motion, except in coincidence with and as a part of the

pharyngeal wall. In the simpler species it is a deflector guiding the air to the dorsal aspect of the pharynx, with or without a sphincter to enclose a spout-like epiglottis projecting through it. The slight mobility of the palate in the monkey is indicated by the median septum on its dorsal aspect, joining the length of the palate to the basicranium.[38] In contrast with the general mobility of the oral and pharyngeal area in this species, there is no possible caudad or ventro-caudad displacement of the central portion of the palate. In species having a more highly developed upper pharynx, the palate has a specialized extrinsic musculature consisting of a levator and a depressor (or tensor) converging upon it, as well as comparatively elementary palatopharyngeus muscles. The levator and palatopharyngeal muscles act in countertraction, though not in functional opposition, to the superior constrictor muscle.[25,66-68]

In homologic comparison among many species, there is evidence of correlated anatomic pattern of palate and epiglottis by which air penetration through the pharynx is facilitated.[3] The anatomic and physiologic adaptations of this region in species accomplishing unusual methods of feeding and respiration is a fascinating study. These correlative adaptations have been extensively reviewed and illustrated by Negus,[4-11] Nemai,[12] Howes,[69] and by Rückert.[34] Thus, in the porpoise and in the newborn marsupial, a spout-like epiglottis penetrates an orifice in the palate, whence it is actively enclosed by a sphincteric arrangement. A further motor arrangement providing for stabilization of the spout-like epiglottis in relation to the palate is that of the epiglottidean muscle which joins the epiglottis to the hyoid and to the tongue and acts in opposition to the palatal muscles. This muscle is particularly developed in the whale, and is found also in several other mammals.[6] In the newborn pig, the epiglottis is short and the palate extends caudad to approximate it. In the first six months of postnatal life, the epiglottis is said to elongate and penetrate to the epipharynx.[70] Most mamalian species, such as the cat, dog, and monkey, apparently retain essentially their infantile pharyngeal proportions.[38] In the higher apes, the pharynx becomes relatively enlarged but is much less capacious than in the mature human.[11]

The upper pharyngeal area of the human infant is compact (Fig. 5), with the relatively large palate occupying much of the area and leaving a narrow slot as the epipharyngeal passageway.[71-73] Bowles[70] has observed that the uvula "fits exactly into the excavated summit of the epiglottis," but apparently this opinion is based upon anatomical dissections of stillborn infants in whom the pharyngeal region has been compressed incident to maternal labor. Roentgen

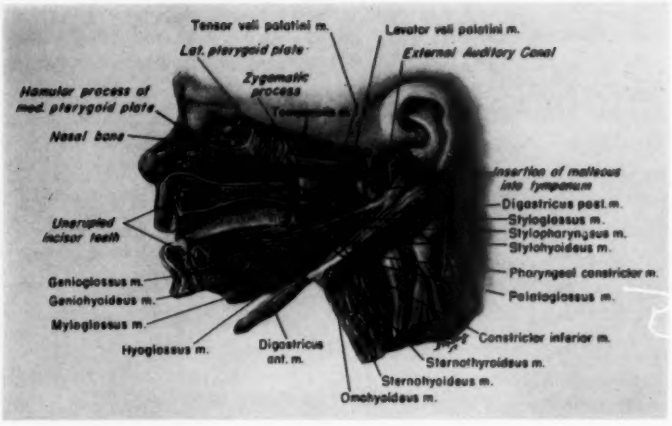

Fig. 6.—Lateral view of supporting muscles of tongue and pharynx in human infant.

studies of living newborns show the palate and epiglottis to be separated into a more expanded pharynx.[74] At rest and during suckle the palate is in approximation to the pharyngeal portion of the tongue. The roof of the infant's pharynx arches gently from the choanae to the dorsal wall of the mesopharynx. Thus, no portion of the upper pharynx can be differentially labelled dorsal or "posterior" wall in this stage of development. The postseptal border of the vomer is in nearly transverse plane.[71,75]

The plane of the eustachian tube and closely related levator veli palatini muscle of the infant is essentially at right angles to the cephalocaudal axis of the body proper (Fig. 6), with the orifice of the tube being approximately on the level of the soft palate.[71,72,76,77] There is little cephalad displacement on the palate incident to performance, except for its slight elevation by the liquid bolus in transit between the tongue and the palate.[3]

In postnatal maturation, the upper pharynx of the human deviates progressively from the basic mammalian pattern. It enlarges in size, displaces caudally and progresses in mobility in relation to the cranium and cervical structures and in mobility of the palate within the pharynx. The anatomic enlargement of the upper pharynx reflects changes in orientation, alignment, and diameters of the basi-

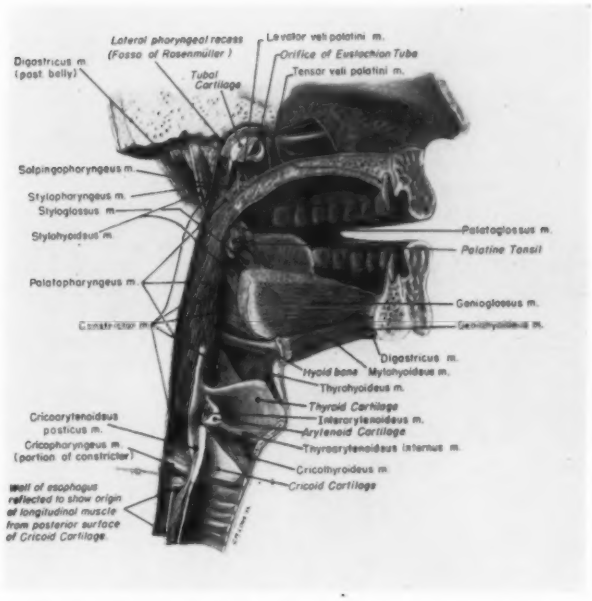

Fig. 7.—Sagittal view of mouth and pharynx in human adult.

cranium, vertebrae and facial skeleton (Figs. 7 and 8). The form of the pharynx is not determined by form or motions of the palate,[78] except when lack of fusion allows a lateral flaring of the pterygoid plates with concomitant increase in transverse dimension.[79] The differential growth of the craniocephalic region, by which the human-distinctive craniovertebral angle is acquired, and the distinctive cephalocaudad elongation of the face are critical in the acquisition of the large volume and cephalocaudal orientation of the pharynx of the mature human. The effect of this acute craniovertebral angulation is a general transverse orientation of the face compared with the vertical orientation of the neck and trunk.[7] This results in a corresponding rectilinear relation of the nasal cavity and upper pharynx. This change is distinctively a human circumstance, as the mature form of other primates retains gradations toward directional continuity of nose and pharynx.[6,11]

Expansion of the antero-posterior diameter of the pharynx during the first year of life reflects dorsad displacement from growth at the

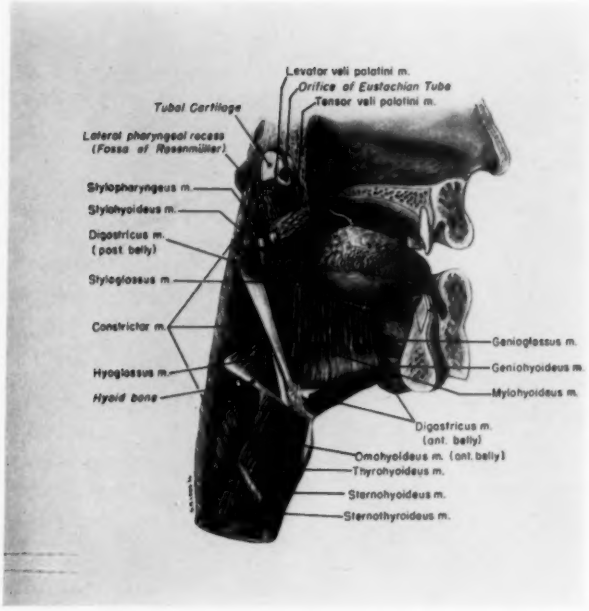

Fig. 8.—Lateral view of supporting muscles of tongue and pharynx, human adult.

spheno-occipital synchondrosis[80] and ventrad displacement in relation to the cervical vertebrae from growth at the facial sutures.[81] Subsequent transverse growth of the face is without further ventrad displacement of its posterior or pharyngeal aspects.[82-84]

Cephalo-caudal elongation of the face, and its corresponding descent from the basicranium, continues throughout human growth.[6,11,85] It is relatively less than elongation of the pharynx, so that the hypopharynx and the larynx extend further caudad, to become enclosed within the neck.[5,77] The relative position of the palate within the pharynx is determined by the descent of the hard palate. One circumstance of potential developmental discrepancy is the independence of facial and pharyngeal growth rates (see below).

The spatial relation of the palate to its extrinsic musculature is also changed during development. The palate descends in relation to the origin of the levator veli palatini, which is on a small prom-

inence of the basicranium at the lateral end of the eustachian tube. Accordingly this muscle, actually a tensor of the palate in its position within the infant pharynx, now becomes a levator. The descent of the hard palate within the face is relatively greater than that of the hamular processes of the pterygoid bones,[83] so that the tensor veli palatini, which was in infancy a depressor of the palate, becomes a tensor.

During the feeding of infants, and of older subjects in supine position, the tensor veli palatini participates in formation of the retro-oral portal by depressing the palate to appose the dorsum of the tongue. This caudal direction of traction of the tensors upon the palate is well-demonstrated in lateral radiographic studies. The position and direction of traction of the tensor muscles may also be noted in the unusual clinical circumstance of contracture of these muscles, as a complication of "bulbar" poliomyelitis.[63,64] In association with developmental changes, the palate is also elongated, particularly that portion distal to the insertion of the levator muscles, as this insertion is indicated by palatal angulation during activation.

The transverse diameter of the pharynx is the dimension least increased postnatally[79,86] and thus reflects early maturation of the midportion of the basicranium. Transverse growth of the pharynx is grossly in parallel to that of the dorsal portion of the nasal cavity and of the mouth. This increase is also coincident with the general lateral displacement of the middle ear and eustachian apparatus. There is extensive change in form of the lateral wall of the upper pharynx, reflecting development of the eustachian apparatus. The orifice of the eustachian tube descends, the tubal cartilage intrudes as the "torus tubarius" into the upper pharynx, and the salpingo-pharyngeal fold suspended from this cartilage becomes apparent.[87] The area of insertion of the palatopharyngeal folds and musculature upon the lateral pharyngeal wall also expands, so that these folds change from their infantile shelf-like contour to that of broadly based buttresses.

In association with this pharyngeal elongation, its further alignment with the cephalocaudal axis, straightening of the dorsal pharyngeal wall and descent of the ventral palatal attachment, there is a general increase in size of the upper pharynx.[84] This increase is much greater than that of the lower pharynx.

Despite comprehensive roentgen cephalometric quantitation and proportion descriptions of the facial area, there is relatively little

normative data pertaining to the upper pharynx.[81,88,89] Cephalometry has been utilized in descriptions of the contours of the basicranium and posterior aspects of the face, comparing the standard points of basion (as identified by laminagraphy), sella turcica, and posterior nasal spine.[89-91] The thickness and length of the soft palate have also been quantified.[79] The transverse diameter of the pharyngeal aspect of the facial skeleton has been compared at the hamular processes in normal and cleft palate subjects,[79] but the normalcy of the transverse diameters of other portions of the pharynx, such as the internal nares, are still expert opinions. This lack of precise criteria constitutes a particular problem in descriptions of motions in this area, as will be noted in later sections of this review.

A further limitation in the description of the volume and diameters of the upper pharynx results from the presence of the pharyngeal tonsil or "adenoid." This follows the lymphoid pattern of development, growing rapidly in infancy, and more slowly in childhood to reach maximum at approximately ten years, after which it usually diminishes slowly to insignificance.[92] The adenoid mass essentially compensates for growth of the epipharynx and modifies the effective dorsocephalic contour of the pharynx coincident with change in craniovertebral angulation. Adenoidectomy effects an abrupt change in volume of the upper pharynx and the palate-pharynx relationship, by which anomalous or neurogenic deficiencies in the relationship may be made apparent (see below).[67,93-95]

The adenoid mass has been commonly indicated as a factor in physiologic incapacity of the upper pharynx, supposedly causing obstruction of the nasal portal of respiration and of flow of secretions from the eustachian apparatus.[96-98] The adenoid mass has been thought to be indirectly responsible for deficiency of transverse growth in the facial region. This relation has been extensively studied in England and the conclusions, as published by Brash *et al.*[99] are: "There is no satisfactory proof that the presence of adenoids, the diminution or absence of nasal breathing or the constant habit of mouth breathing can affect the form of the jaws or the position of the teeth in any of the ways that have been suggested. It has still to be proven that there is any significant correlation between the presence of adenoids and the incidence of deformities of the jaws and palate." This interpretation is supported from observations of normal facial growth despite atresia of the posterior choanae[100] or tracheotomy[55] prolongedly in childhood.

The changes in pattern of motor function of the upper pharynx are of greater physiologic significance than the changes in its relative

diameters. With maturation, the pharynx in general becomes more mobile, and the palate more mobile within it.

An actual diminution in attachment of the retropharyngeal median raphe joining the pharynx to the prevertebral fascia occurs. In the human infant, as in lower mammals, such as the rat,[40] a distinct fascial raphe joins the length of the posterior pharyngeal wall to the prevertebral fascia and to the vertebrae though ventral displacement of the dorsal wall does occur, as in swallow. The mobility of the human infant pharynx generally is facilitated by the sling arrangement of the stylohyoid appartus, which in many other mammals is a continuous articulated skeleton (see above).

The mobility of the palate increases even more than does that of the pharynx. This is made possible by expansion of the cavity of the upper pharynx, and also reflects the change in cephalocaudal alignment of the palatal extrinsic musculature. This mobility is reminiscent of that acquired by the tongue within the correspondingly and simultaneously expanded oral cavity, though movement of the palate occurs only in a median plane, without lateral deflection.

The motor performance of the upper pharynx in its homologic variety of forms and arrangements requires and depends upon adaptations of its structures. The variations in the most cephalic portion of the constrictor musculature and the related palatopharyngeus-levator musculature, and in the stylohyoid skeleton and musculature, have been mentioned previously. There is also performance-appropriate adaptation of the pad of collagenous connective tissue which forms the internal structural support of the palate. The physical character of this pad is exaggerated in the preserved human cadaver, in which it is much more firm and resistant to passive bending than in the living or recently deceased subject. In the human, this pad is supplemented by a median rib or strut providing reinforcement appropriate to the greater mobility of the palate within the expanded upper pharynx. This median strut is associated with a prominent uvula and also with intrinsic "uvulae" or azygous veli, medialis veli[58] and levator veli medialis[101] muscles which extend linearly beside it, some of them terminating in the soft tissues of the uvula.

The human uvula is comparatively large and of distinctive histologic and neurologic composition. The vascularity, the number of papillae with accompanying "organized" nerve ending, as well as the small nerve bundles in the dermis are all greatly increased in comparison with the hard or soft palate.[103]

The innervation of the upper pharynx is apparently homologically similar. Sensation is conveyed by the glossopharyngeal nerve, and is principally tactile in elicitation—there being no proprioception in the pharyngeal musculature,[3] and no olfaction, though this sensation is adjacent in the nose and in some species in the tip of the epiglottis.[4-11] There has been no correlation of sensory elicitation in the human palate with histological study of nerve endings.

Motor innervation of the upper pharynx is from the nucleus ambiguus, variously conveyed in the glossopharyngeal or vagus nerves.[102] These innervations are variably intermixed in a "pharyngeal plexus," which is subject to much interspecies variation.[103] The question of whether the upper portion of the human pharynx receives its motor innervation from the glossopharyngeal (IX) or from the vagus (X) nerves has continued to be a difference of opinion. Patients examined following surgical glossopharyngeal section, for relief of glossopharyngeal neuralgia or tic, demonstrated no motor impairment in the pharynx.[104,105] Nickl[106] distinctively found that galvanic stimulus to the chorda tympani branch of the facial nerve caused elevation of the soft palate in sixty of his patients. This is in contrast with the observations of Beevor and Horsley,[107] that "in macacus sinicus, movements of the palate occurred in intracranial stimulation of the vago-accessorius and did not occur on intracranial stimulation of the nerve facialis." *In vivo* stimulation studies and anatomical dissections of guinea pigs, dogs, cats and apes by Rethi supported this view. The motor innervation of the tensor veli palatini is from the trigeminal nucleus and nerve.[109]

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(Part II, Physiology, will follow)

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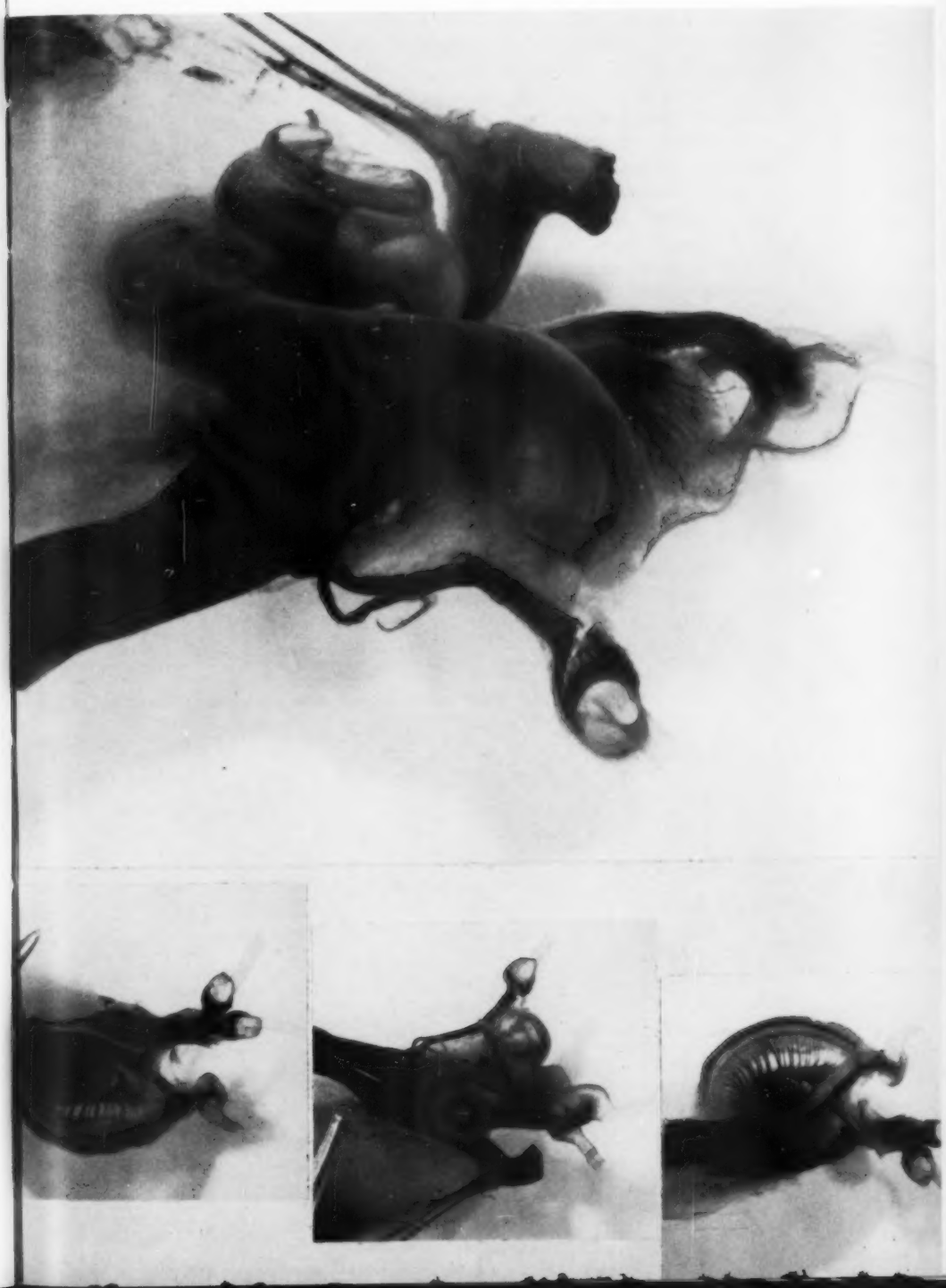
"MEMBRANOUS INNER EAR"

This remarkable photograph of a superb dissecti received two top awards in a recent annual exhibit of the Biological Photographic Association.

The First Prize of the Association was given to the photographer, Mr. Arthur J. Bowden of the Henry Ford Hospital, as the best exhibit in the category "Specimen, Monochrome Prints." Mr. Bowden received also the Special B.P.A. Medical Education Award, presented jointly by the Association and *Postgraduate Medicine*, a national medical publication, "for medical photography having superior educational value."

The dissection was done at Henry Ford Hospital by Dr. Richard Gacek and Dr. Harold Schuknecht who is now Head of the Department of Otolaryngology at Massachusetts Eye and Ear Infirmary, Boston.

—*Courtesy the Biological Photographic Association*



LXXI

CLINICAL TESTING FOR SOUND LOCALIZATION

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With recently increased knowledge of the neurology and physiology of directional hearing, sound localization testing is offering possibilities of practical applications in clinical diagnosis. Many different methods of testing are being used, however, making it difficult to evaluate and integrate the increasing clinical data. In many cases the extensive outlay of equipment is prohibitive for use except at a research center. It is the object of this paper to evaluate methods of measuring sound localization, with emphasis on possible practical simplification of the required equipment.

THEORIES OF SOUND LOCALIZATION

Out of the variety of experiments and studies to explain the mechanisms involved in sound localization, several definite theories have been postulated.

The intensity theory, one of the oldest, is based on the principle that when sounds varying only in intensity are lead to both ears simultaneously, the observer will tend to localize the sound to the side of the greater intensity. Studies such as done by Firestone[6] with wax models of human heads with microphones in the ears, showed the expected smooth change of amplitude with azimuth on frequencies below 1000 cycles. Irregular curves on higher frequencies were thought due to interference or reinforcement patterns of out-of-phase sounds passing in front of and behind the head to the opposite ear. Intensity difference due to inverse square law effects is greater for sounds arising close to the head, and insignificant for distant sounds. Experiments such as those done by Sandel et al.[30] by measuring intra-aural sound intensity with calibrated sound probes in the ears show

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an increasing difference in level between the near and far ear as the frequency increases. Values varied from about 5 db for 500 to 1750 cycles to 9 db at 5000 cycles. This constitutes the increased "shadow effect" of the head for high frequencies where there is a greater ratio of the diameter of the head to the wave length of the sound. Jongkees and Groen[9] demonstrated that decreasing the auditory acuity in one ear 20 db with a wax-cotton plug caused a displacement of subjective impression toward the normal ear, but that this effect decreases in several hours and becomes very slight in twenty-four hours. After the adaptation had taken place removal of the plug caused a brief displacement to this ear that quickly readjusted to normal. These findings support the generally accepted opinion that the role of intensity difference is manifest at higher frequencies.

The time-difference theory is based on the principle that when two sharp sounds varying only in time are led to the two ears of an observer, he will tend to localize the sound as coming from the side of first arrival. The phase theory is based on the observation that when two continuous tones varying only in phase are led to the ears of an observer, he will tend to localize the sound as coming from the side of the leading phase. The only difference between these theories is that the time-difference theory depends on the time of arrival of a single sound, while the phase theory depends on the time of arrival of the wave of a continuous sound. This is well illustrated in the diagrams (Fig. 1) by Kietz[14] showing the directional sensation of various phase relationships of 800-cycle continuous tones, with an abrupt reversal of the directional sensation when the phase difference exceeds one-half wave length. This reversal could not occur in human ears at or below 800 cycles, as a half wave length of an 800 cycle sound is 21 centimeters, which is equal to the maximum difference in sound path from the near to far ear. In the case of sounds of frequency higher than 800 cycles, this reversal of the directional sensation would occur. At these higher frequencies a given phase relationship between sounds in the two ears could correspond to that of sounds arising from more than one azimuth, making sound localization by phase difference impossible. Jongkees and Groen[9] confirmed this on perimeter tests showing that sinusoidal tones over 1000 cycles were difficult to localize. As pointed out by Kietz, it is certainly no accident that the human refractory period of the auditory nerve is exactly of such a value (Davis et al.) to prohibit temporally accurate transmission of tones above 800 cycles. He assumed that an elephant with his much broader head would have his refractory period so constituted that phase localization is possible only for tones up to 200 to 400 cycles.

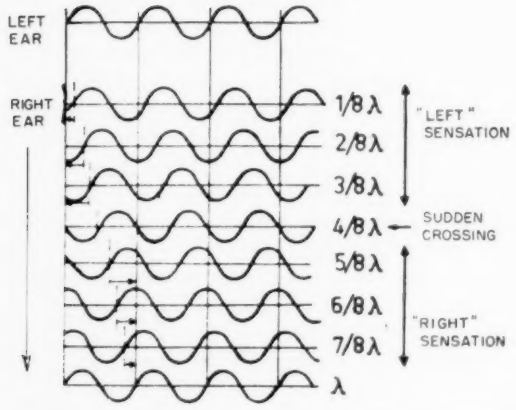

Fig. 1.—800-cycle continuous tone showing directional sensation with interaural phase shift. (From Keitz[14])

The work of Stevens and Newman[37] showed that the ability to localize pure tones varied markedly with their frequency, being good below 1000 cycles, becoming worse between 2000 and 4000 cycles, and better again above 6000 cycles. These findings are explained by the localization of low frequencies by phase difference, and the higher frequencies by intensity. Wightman and Firestone[36] demonstrated that complex sounds, such as a click or a hiss, were localized more accurately than a pure tone, and attributed it to the fact that complex sounds contain both low and high frequencies.

Keitz[14] explained the experimental finding that the accuracy of function of localization, as indicated by the minimum perceived time difference, is much greater at 800 cycles and progressively decreases as the frequency decreases to 200 cycles. This is correlated with and explained graphically by the fact that the slope of the wave ascent is greater with higher frequencies; in fact it is four times steeper at 800 than at 250 cycles, resulting in a more abrupt sound impulse and more accurate time difference perception. Abrupt complex noises could also be expected to be localized more accurately by this reasoning, as well as by their wider range of frequency.

It should be pointed out that other factors are involved in lateralization of a tuning fork or bone-conduction receiver on the skull. Spoor, Schmidt, and Van Dishoeck[31] demonstrated that a 500 cycle

receiver could be placed to the right of the midline of the skull in a critical position and produce lateralization to the opposite ear. In this case pick-up of skull vibration, plotted with a vibration detector showed a minimum pick-up at critical points in the ipsilateral ear, indicating that the bone conduction lateralization was due to interaural intensity relations affected by vibration patterns in the skull rather than by interaural phase.

The change in loudness and quality of sounds with turning of the head has long been recognized as a means of localization as to position in front, behind, or over the observer's head. Klensch[15] performed experiments with funnels on tubes to each earpiece of a stethoscope. If the funnels were moved past a sound source in front of the observer without head movement, the sound was displaced but not localized. If the head were turned with the funnels the sound was localized correctly in front. If the tubes were crossed with this procedure, or if the head and the funnels were moved in opposite directions, the sound was localized behind the observer. It was shown that only ten-degrees movement of the head afforded localization. Wallach[34] arranged 20 radially placed speakers about an observer with a twenty-contact radial switch turning with the observer's head, so that the speaker directly in front of the observer was always on in any head position. The observer localized the sound vertically above his head with turning and retained this localization when the head was held still. By arranging an artificial head with microphones for ears amplified to receivers in the corresponding ears of the listener, and with a mechanical system so that when the listener's head turned the artificial head did likewise, Koenig[17] showed that the listener could correctly localize the sound. Without the artificial head movement, the listener localized the sound in an azimuth behind him, never in front. Jongkees[12] studied the directional localization on ten patients with total unilateral deafness, and found two with essentially normal and one with nearly normal directional localization. He attributed this localizing to perception with small head movement and shielding effects of the auricle.

The importance of head-turning is stressed by Christian and Röser[4] in sound localization by persons with more than thirty decibels difference in hearing in their two ears.

The possibility has been explored that the vestibular apparatus may play a role in sound localization. Meurman and Meurman[22] found that bilaterally fenestrated patients made many more errors in sound localization than did normal subjects, and speculated that

semicircular canals might play a part in directional hearing. Koenig and Sussmann,[16] and Jongkees[12] however found normal directional hearing in patients whose vestibular function was destroyed by streptomycin without deterioration of hearing.

The pinna is credited with helping in directional hearing by causing differences in intensity and tonal qualities of sounds in front and behind, and also with changes in head position. This is thought to be more effective for complex sounds with which the observer is familiar, and with high frequencies for which the pinna casts more of a "sound shadow."

THE CENTRAL NERVOUS SYSTEM IN SOUND LOCALIZATION

The explanation of central nervous system mechanisms in sound localization is more difficult than the better understood peripheral factors that have been discussed, and requires evaluation and integration of neuroanatomical, otophysiological, and electrophysical investigations.

The detailed anatomy of the auditory pathways in the cat described by Lorente De Nó[18] in 1933 demonstrated an extensive group of fibers in the cochlear nucleus that radiated centrifugally from the higher auditory pathway nuclei into the cochlear nucleus where they branched out, and are probably part of Rasmussen's olivo-cochlear tract. Jungert[13] did detailed electrophysical mapping of auditory pathways in the cat measuring latency of responses with micro-electrodes and measured the refraction time of the central auditory pathway as 2 msec.

In experiments on cats that were conditioned to directional responses Neff et al.[24-26] demonstrated that bilateral destruction of the auditory cortex greatly impaired directional localization, while the ability to differentiate pure tone pitch could be trained again. Other clinical correlations with central nervous system function are indicated by the findings of Matzker and Springborn[20] who tested directional hearing on 117 normal persons between the ages of 5 and 80 years, and found a steady decline past the age of 40 years correlating with presbycusis. Rousey and Goetzinger[27] demonstrated that stuttering subjects gave impaired localization responses.

It has been a problem to explain central nervous system discrimination of the small time intervals involved. Mills[23] demonstrated a minimal azimuth discrimination of only one degree, which represents

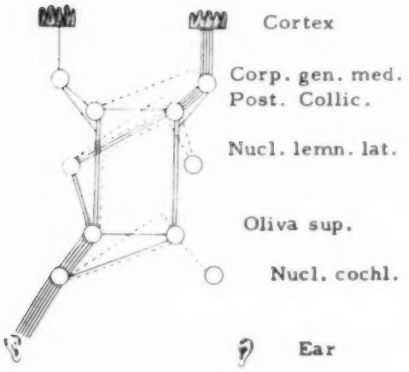

Fig. 2.—Central auditory anatomy diagramming facilitating and inhibiting pathways. (From Matzker[19])

an extremely small time interval, and on standard tests normal subjects localize with time differences of less than .02 msec. The range of time difference in localizing sounds is from zero for midline sounds to a maximum of a little over .6 msec for sounds 90 degrees off the median plane where the time lag is represented by the average maximum distance of sound path between the two ears of about 21 centimeters. This figure approaches the Hornbostel-Wertheimer constant of 0.6363 msec, and with greater time differences the observer still localizes the sound at a 90 degree azimuth until the time difference reaches a value of 2.0 msec (Matzker[19]) to 2.5 msec (Walsh[35]) where instantaneous sounds are perceived as separate sounds in the two ears. The agreement of this 2 msec time with the refraction time of central auditory pathways as determined by Jungert suggests that inhibitory nerve blocking is involved.

Joseph Matzker[19] in 1958 presented a brilliant hypothesis of the mechanism of fine time-difference registration, proposing that the above-mentioned centrifugal fibers of the auditory pathway in the brain stem are elements used for inhibitory processes. Figure 2 from Matzker[19] diagrams only those pathways that transmit facilitating or inhibitory impulses from the right ear and eliminates the pathways from the left ear for clarity. The unbroken lines indicate centripetal facilitating pathways conducting stimuli to the cerebral cortex, and the inhibitory paths are shown in dotted lines for uncrossed tracts and

dashed lines for crossed tracts. As the synapse time of 0.6 msec is necessary before an inhibitory effect can be achieved, it is assumed that the inhibitory crossings are arranged in such a way that an inhibitory neuron of lower order, such as a second neuron, influences a neuron of higher order, such as a third neuron, on the opposite side. This permits inhibition of the impulse from the opposite ear with a time difference of less than 0.6 msec. The uncrossed inhibitory fibers shown in dotted lines pass centripetally to the next higher auditory nucleus on the same side so that even impulses that have crossed from the opposite side at a lower level can be inhibited. As an example of the operation of Matzker's hypothesis, a click reaching ear A 0.2 msec before ear B sends impulses to the auditory cortex predominately on the opposite side. At the same time, however, impulses are sent across the inhibitory pathways arriving at the nucleus cochlearis, the olive, and the nucleus lemnisci lateralis of the opposite side at just the right time to block the synapse before the facilitating impulse of the corresponding stimulus frequency of the later-stimulated ear B, reaches it. As a result the auditory cortex of the later-stimulated ear is stimulated by fewer fibers than the cortex that was stimulated slightly sooner, producing the response of a softer sound. It is this loudness difference that makes directional perception possible.

There is confirmatory evidence of such a mechanism by the observations of Kietz[14] with sounds that can be led to separate ears with independent control of intensity and time. If an in-phase sound is made 15-20 db louder in one ear the listener lateralizes the sound to this ear. Without changing the relative intensity the sound to the other ear can be advanced in time so as to repel the lateralization due to loudness and return the localization to the midline.

DIRECTIONAL HEARING AND SPEECH DISCRIMINATION

There is increasing evidence that directional hearing facilitates the intelligibility of speech especially in the presence of noise. Belzile et al.[1] showed on testing both conductive and perceptive deafness groups that 50% discrimination can be achieved in the presence of 10 db more noise when wearing a binaural hearing aid than with a monaural aid. Hirsh[7] found that the speech reception threshold could be lowered in the presence of noise when the sound and noise sources were separated so that the listener could use directional hearing to discriminate against the noise. Wright[37] suggested that there could be an auditory "squelch" effect to account for observations that sudden sounds are less disturbing to a listener when both ears rather than one are used. The inhibitory-fiber hypothesis of Matzker could ac-

count for such a mechanism operating below the threshold of a crossed stapedial reflex. Koenig[17] demonstrated the beneficial effect of directional hearing on speech intelligibility with noise by the following experiment: binaural receivers with separate amplifiers were connected so they could be switched to either a single microphone or to spaced separate microphones for directional hearing. With directional hearing there was improved discrimination in the presence of noise, and the listener had better intelligibility for one of several simultaneous conversations.

Some correlations between binaural versus monaural hearing and increased discrimination scores can also be accounted for on the basis of "binaural summation and integration." Recent developments in such speech testing by introducing distorted or incomplete frequency spectrum sound in one ear, or with sound in the other ear to complete the spectrum, illustrate mechanisms of increased discrimination (Bocca,[2,3] Jerger,[8] and Matzker[21]). These tests have also shown promise in localizing central auditory lesions particularly in the temporal lobe.

CLINICAL SIGNIFICANCE OF IMPAIRED SOUND LOCALIZATION

Sanchez-Longo and Forster in 1957[29] performed perimeter sound localization testing with 120 cycle tone and pointing to indicate the position of the sound on normal patients and on five patients with temporal lobe lesions. All five patients with temporal lobe lesions demonstrated impaired localization ability in the contralateral field. Later studies were done by Sanchez-Longo et al. in 1958[28] on fifty patients with various intracranial lesions. Eighteen out of twenty patients with temporal lobe involvement showed impaired sound localization in the contralateral auditory field, and only occasional cases of frontal lobe, cerebellar or basal ganglia lesions presented abnormal tests.

Using median plane localization band testing with electrically controlled interaural time differences in 14 steps between .018 msec to 0.648 msec, Matzker[21] tested with audiometer tones from 250 through 6000 cycles. In some cases abnormal localization was limited to one or a few frequencies, and abnormalities were found with brain stem and frontal, parietal, and occipital lobe lesions as well as with temporal lobe lesions. In lesions above the ventral brain stem deviation of localization points to a contralateral lesion, and below this point to a homolateral lesion. In both series of cases pure tone audiograms were not of diagnostic or lateralizing significance.

METHODS OF SOUND LOCALIZATION MEASUREMENT

As well as the two methods described above many means of measuring directional hearing have been used.

Sandel et al.[30] devised a system with a movable speaker to be used to indicate the position of a fixed speaker, eliminating the factor of pointing by the patient. A loud speaker on a four-foot beam with an electric motor to control rotation, was used by Viehweg and Campbell[33] on careful tests conducted in quiet rooms. They found that noise impaired localization from 87 to 84% in normally-hearing patients and from 44 to 36% in monaurally impaired patients. Christian and Röser[4] used an elaborate electronic set-up with three separate rooms. They produced a measured time difference in sounds to the two ears by varying the distance of two separate microphones from a loud speaker sound source. The two microphone outputs were separately amplified with controlled and equalized circuits so that sounds of varying time difference and equal volume could be delivered to balanced receivers.

Jongkees and his associates[9-11] performed careful studies of the use of compact perimeter testing. They used 50 to 60 cm radius perimeters and had blindfolded patients with their heads held still in a chin rest point to the apparent location of pure tone or noise sound sources. They devised a graphing method as used in Figure 4 in which objective azimuths are charted as ordinates and subjective azimuths as abscissas on rectangular co-ordinates so that the normal "curve" would be the 45 degree axis. In actual testing they found that normal patients consistently pointed outside the correct position in the mid-lateral field as shown in the solid line curve in Figure 4 producing a reversed-S curve of sufficient deviation from theoretical normal to stimulate investigation. The "S-curve" was less marked with white noise than with pure tones. It was suspected that the error was due to the fact that the auditory axis was near the center of the head and that the proprioceptive arm-pointing axis was at the homolateral shoulder, but having the patient point in the right field with his left hand made no difference. Suspecting that the pinna effect was a factor, 6 cm tubes were placed in the listener's ears and it was found that the "S-curve" was increased rather than decreased.

EXPERIMENTAL APPROACH TO SOUND LOCALIZATION TESTING

Waveform. Before starting evaluation of perimeter testing it was considered advisable to determine the best type of sound to use.

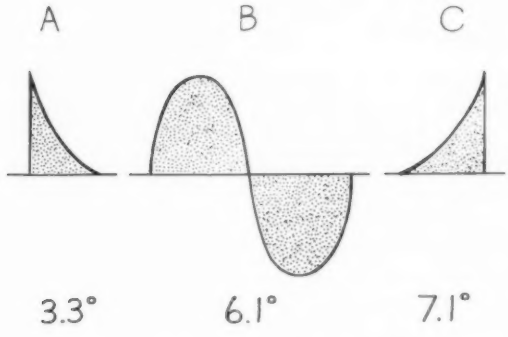

Fig. 3.—Accuracy of localization of 1000-cycle sounds of different wave form. A. Saw-tooth wave with instantaneous rising phase and exponential fall. B. Sinusoidal wave. C. Saw-tooth wave with exponential rise and instantaneous fall.

Kietz[14] stated, "It is unknown whether the insertion of the impulse group or the presumably more abrupt termination of the nerve impulses is utilized for localization." This raised the question whether it was the leading or trailing waveform that was important. With the general findings of better localization for noises and complex sounds a saw-tooth generator was used which was designed to provide a variable frequency using a gastriode oscillator. Output circuits were designed to provide output of wave form as shown in diagrams A and C in Figure 3. In A there is an almost instantaneous rising phase and exponential fall, and in C there is the reverse. This waveform is as shown when a purely resistive load is used and may be distorted with a reactive load, so the output circuits were resistively swamped to more closely approximate the desired wave form. The test tones were electronically switched back and forth between two 1.5 inch diameter loud speakers at second intervals using an a-stable multivibrator with square-wave output to control the switching frequency. A 50 cm diameter perimeter scale was used similar to that used by Jongkees, except that one speaker was held at various azimuths to be tested and the patient moved the other speaker on a radially moving arm until the sound seemed to be coming from a single point. The listener's eyes were closed and his head held still on a head rest.

The reference speaker was used instead of pointing so as to eliminate the problem of the S-curve of Jongkees, and to eliminate

possible errors from pointing. As pointing is a proprioceptive and not an auditory space perception, and the testing of patients with pastpointing and proprioceptive impairment was anticipated, sound reference was preferred.

Five normal subjects under the age of 45 were tested on the nine central 10 degree azimuth points. The extreme lateral fields were not used based on the findings of Mills[23] that differential azimuth discrimination varied from a minimum angle of one degree straight ahead and increased rapidly in the lateral field and at 90 degrees is almost indeterminate. Based on 45 observations with each type of noise at the approximate frequency of 1000 cycles the results showed the most accurate localization of 3.3 degrees for the instantaneously rising saw-tooth wave, 6.1 degrees for sinusoidal waves, and 7.1 degrees for the exponential rising saw-tooth wave. Actually the two forms of saw tooth waves sounded almost identical in quality, and it was striking to see the uncertainty of the subject in localizing sound C after being tested with sound A. This indicates that a sound impulse group with a more abrupt insertion wave form is more easily localized, and suggests that the answer to the question raised by Kietz is that it is the insertion time of the impulse group rather than the more abrupt termination of nerve impulses that is utilized for localization.

This principle has practical application in the design of sound sources that can be easily localized. A notable example of need for this is in warning signals for emergency vehicles, and evaluation of the siren in common use shows that it leaves much to be desired. The gradual amplitude and frequency modulation of the siren sound provides no abrupt sound impulse groups to permit accurate localization. Tests with recorded siren noise through perimeter speakers showed that the sound was difficult to localize. The psychological effect on a motorist of hearing a siren that he cannot localize is a brief sensation of panic while he frantically looks in all directions to locate the emergency vehicle, and valuable seconds may be lost in clearing the right of way. On several occasions the writer has noted that the siren of an approaching fire engine could not be localized until the bell was rung, and that the direction was immediately apparent on hearing this abrupt sound pattern. The design of emergency sirens might be improved if the sound could be abruptly modulated to facilitate ease of localization.

INVESTIGATION OF THE S-CURVE

Feeling that it should be possible to account for the S-curve of Jongkees, his experiments were repeated with five normal subjects on

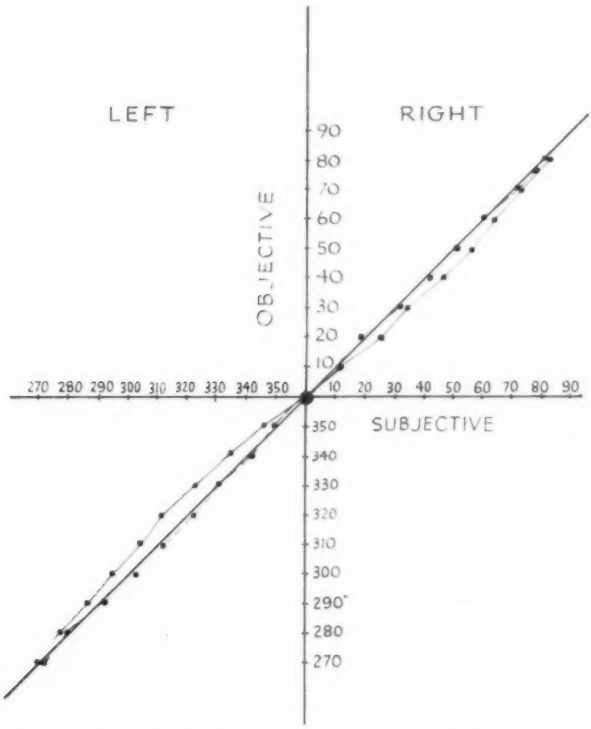

Fig. 4.—Sound localization of 800-cycle instantaneous-rise saw-tooth tone with 50 cm radius perimeter using a reference speaker. The solid line shows the results by the conventional test, and the broken line shows the results with a transverse head shield.

a 50 cm diameter perimeter using 800 cycle abrupt-rise saw-tooth sound. One-half second pulsing was used with a single speaker, as pulsing seemed to further facilitate localization as well as the fact that with the short pulses the patient could not gain any practical positional information if he turned his head slightly. The results as shown in Figure 4 in the solid line confirmed the S-curve as described by Jongkees.

The first possible explanation for this curve that was investigated was that cortical perception of temporal differences between the ears is undoubtedly based on sounds from essentially infinite distance.

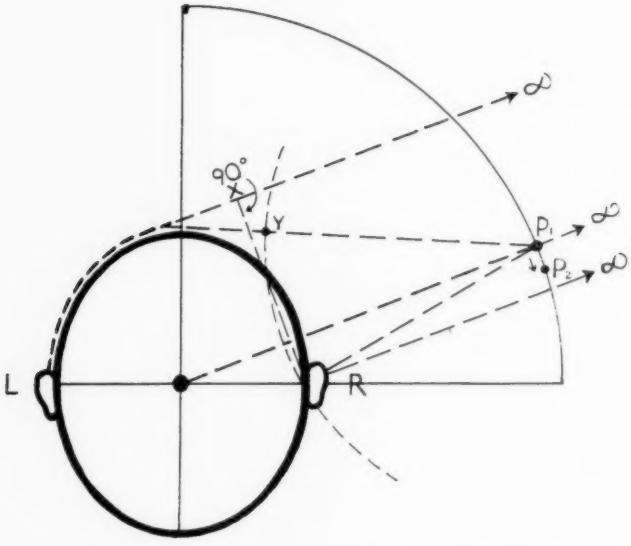

Fig. 5.—Diagram showing varied difference in sound paths to the two ears from points on the same azimuth at infinite and near points.

In Figure 5 the distance from the left ear to point X represents the difference in path to the two ears from parallel sound paths from an essentially infinite sound source. P_1 represents a close point of the same azimuth, and the distance from the left ear to point Y represents its difference in sound path to the two ears.

As shown by the diagram this is a greater difference in sound path, and it would be expected that the brain perceiving sounds as of infinite origin would interpret the close sound as being displaced more laterally toward P_2. This might account for some of the central portion of the S-curve and it was suspected that the extreme lateral field return toward the objective axis might reflect the innate inaccuracy of testing in this area.

To measure this error a model of a cross section of a human head was set up on a 50 cm perimeter circle, and strings were carefully stretched from the position of the ears to points on the perimeter, and parallel to radial azimuth lines for the infinite positions, so that measurements of LX and LY could be carefully taken. These are

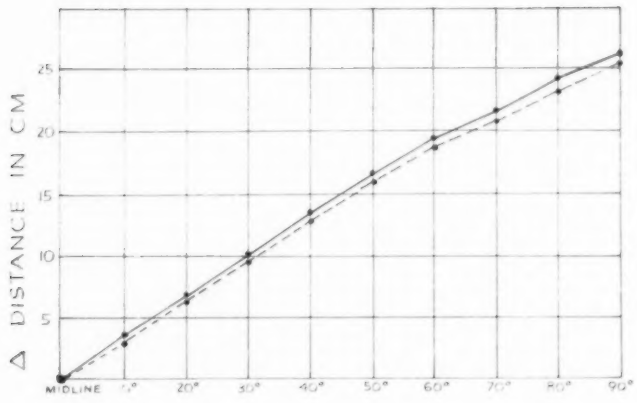

Fig. 6.—Graph of the difference in distance to the two ears at various azimuths from a point at 50 cm distance shown by the solid line, and from an infinite point shown by the broken line.

charted in Figure 6, and show the predicted lateral displacement of the subjective azimuth increasing with lateral displacement. In magnitude this amounts to a lateral displacement of about three degrees in the lateral field. The maximum difference in path between the two ears of 25 cm instead of the 21 cm value usually given as an average is due to the fact that a size 7¾ head was used as a pattern for the model.

An inspiration came from the report of Sandel et al.[30] in describing experiments with two speakers a short distance apart simultaneously excited in phase, which produced the subjective response to the listener of sound coming from a single "phantom" speaker between the two. Figure 7 illustrates normal anterior sound paths to the two ears from a near point P_1. In the central portion of this quadrant there would also be a second longer sound path behind the head to the left ear. As the brain is perceiving an anterior localization it would interpret this sound as coming from point Q so located as to produce this greater sound path difference to the left ear by a normal anterior route. This is equivalent to two sound sources in phase at points P_1 and Q, and would produce the subjective response of a single sound at P_2 resulting in the lateral displacement of the subjective azimuth in the central portion of the quadrant, but not toward the midline or laterally where there are equal paths to the opposite ear.

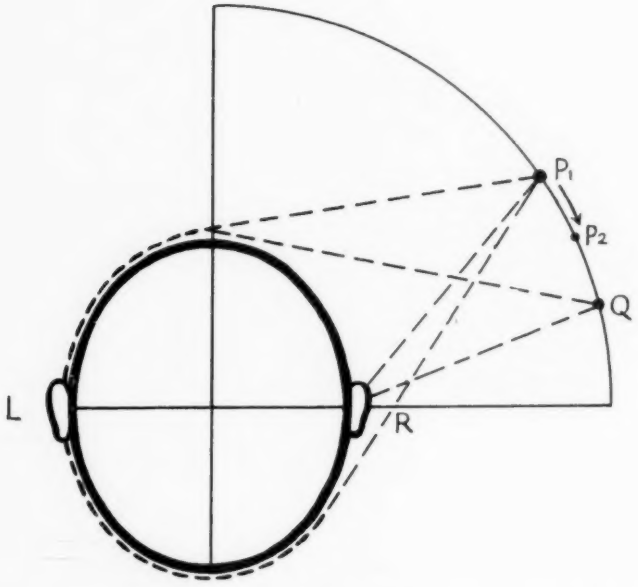

Fig. 7.—Diagram illustrating mechanism of apparent lateral shift of azimuth due to sound passing behind the head to the opposite ear.

To test this theory a large double-layered shield of corrugated cardboard was cut out to fit tightly over the subject's head behind his ears and form a transverse shield to prevent passage of a sound behind his head. With this shield in place on the same five subjects the curve shown in a broken line in Figure 4 was obtained with the elimination of the S-curve. This confirms the theory that a second sound path behind the head as diagrammed in Figure 7 causes the subjective localization displacement accounting for the inverted S-curve in perimetry testing.

EVALUATION OF TESTING METHODS

While short-radius perimetry testing for sound localization offers the greatest simplicity and minimum outlay of equipment, it has a number of disadvantages. Indicating sound position by pointing introduces the additional factor of proprioceptive as well as auditory direction perception and complicates clinical evaluation of impaired

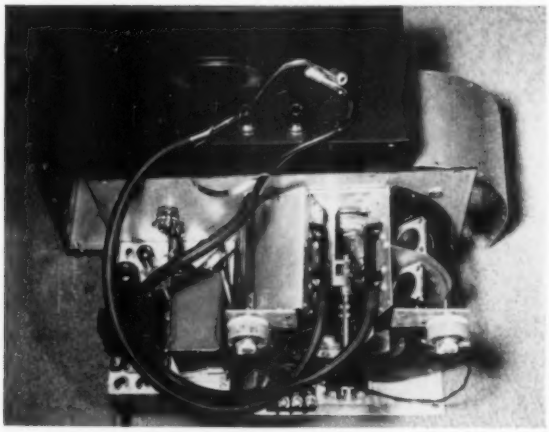

Fig. 8.—Sound localization meter using varied sound-path distances from simultaneously excited loud speakers. The cover has been removed on one side to show details of the speakers.

test results. It is mechanically difficult to rigidly fix the patient's head so as to prevent slightly head movement that is thought to be an important factor in the ability of unilaterally deaf patients to localize sound without bilaterally intact auditory pathways. With use of a short radius perimeter the subjective localization errors due to parallax and mid-field displacement due to a second sound path behind the head described in Figures 5 and 7 are sufficient to practically affect the accuracy of the results. Longer radius perimeters and shielding of the patient's head to prevent sound passage behind it are impractical.

The problems of head movement and spurious sound paths are solved by using earphones or stethoscope ear pieces to introduce sounds separately in the two ears unaltered by head movement.

The time difference between the sounds introduced to the ears can be controlled electrically in steps as done by Matzker,[21] but continuous control of the time difference by methods such as used by Christian and Röser[4] offers the advantage of increased accuracy. With such methods it was found easier to detect and disregard spurious false direction reversal at half-wave length points.

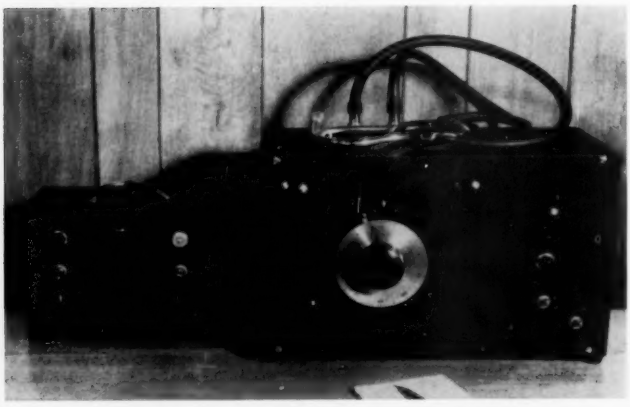

Fig. 9.—Front view of the sound localization meter showing the concentrically mounted dial and movable pointer indicating the positions of the pairs of variable reference and test speakers. The cabinet on the left contains the variable frequency gas-triode saw-tooth wave generator.

The clinical results of Sanchez-Longo and Forster[29] suggested that it might be desirable to test the ability of sound localization in both lateral fields as well as median plane localization. To provide a test evaluating purely sound localization it is necessary to provide a sound reference for comparison with the test sound for both median plane and lateral field testing.

SOUND LOCALIZATION METER

After experimenting with various methods to fulfill these requirements, the test equipment took the final form illustrated in Figures 8 and 9.

Two balanced pairs of loud speakers with each pair excited in phase are used instead of single speakers for the reference and testing speaker. The pairs of speakers are mounted on opposite ends of an incomplete annular ring of aluminum which is turned within an annular case as shown in Figure 8, and each pair is separately rotated in the same axis by a rear offset gear and a front vernier dial. The second one of each pair of speakers is concealed within the shield at the left.

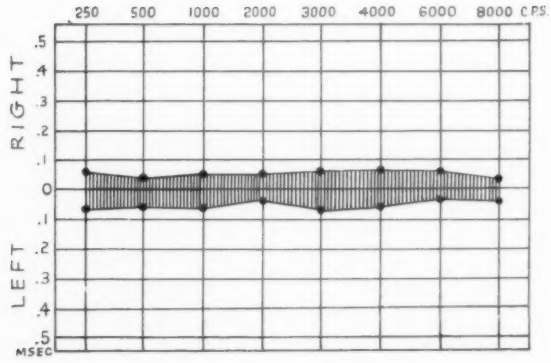

Fig. 10.—Median plane localization chart showing average values for five normal young adults.

Figure 9 shows the front view of the dial and indicator for the two sets of speakers. The testing set of speakers has a rear knob that can be turned by the patient sitting behind the instrument and its settings are read from the pointer on the front panel. With the dial or pointers in the mid-position the paired speakers are equal distance from the funnel openings to the tubes of the stethoscope worn by the patient, and zero time difference or median plane sound localization is produced. Turning a pair of speakers to one side shortens the sound path to that side and lengthens the sound path to the other, so that with a mean radius of the arc of the speakers of 7.9 cm each division on the 0-100 division dial represents 0.03 msec. The pairs of speakers are connected in series with a loudness balancing potentiometer across them so that their loudness can be balanced with the time difference dials in midposition. In lateral positions the sound is slightly louder in the ipsilateral ear simulating reception of sounds from natural sources. The electronic switching circuit using an astable multivibrator with square wave output controls separate amplifiers which supply alternate pulses of sound to the test and reference speakers. Switching of the input circuit permits selection of either saw-tooth or audiometer tone input. Tests can be done for localization with the reference speaker in the midline or at any point in either lateral field and the front dial and pointer indicates the error of the patient's localization. By switching off the reference speakers a median plane localization test as described by Matzker[21] can be done. Figure 10 shows a

median plane localization chart representing average values for five normal young adults.

In doing simple localization tests with an 800 cycle saw-tooth tone no problems were encountered, but in using audiometer tones above 800 cycles it was found that care must be taken to avoid false lateralization reversal points as indicated in Figure 1 at half wave length phase shift. These spurious reversal points are very sharp and their nature is more apparent with the instrument with continuous control of time difference. Figure 3 in Joseph Matzker's paper[21] reports a localization band test showing normal sound localization except for the 1000 cycle frequency where there is a sharp lateralization reversal point in the right deviation range near the 0.5 msec point that represents a half wave length at this frequency. It is difficult to evaluate whether such a result represents pathological localization or a spurious half wave length reversal point. By starting in the median position and turning the dial to the sides until the patient notes lateral localization the true median localization band is charted without confusion. If the test is started from extreme lateral localization, however, the spurious half wave reversal points are encountered above 800 cycles.

SUMMARY AND CONCLUSIONS

1. The literature of sound localization was reviewed with emphasis on clinical testing and evaluation.

2. Experimental investigations in sound localization indicate:

   a. Instantaneous rise saw-tooth sound is localized more accurately than exponential rise saw-tooth or sinusoidal wave form sound. This indicates that the insertion time of the sound impulse group is utilized in sound localization rather than the more abrupt termination of the nerve impulses.

   b. A parallax displacement error of about three degrees results from using a 50 cm radius perimeter.

   c. The midlateral subjective sound displacement laterally in short radius perimeter testing results from a second sound path behind the head to the opposite ear.

3. A sound localization testing instrument that is practical for clinical use is briefly described.

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LXXII

FREE FIELD STARTLE RESPONSE AUDIOMETRY

A QUANTITATIVE METHOD FOR DETERMINING HEARING THRESHOLD OF INFANT CHILDREN

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IKUZO SATO, M.D.

MATSUMOTO, JAPAN

It is universally known that infants respond to sound stimulation by random movements of their eyes, face and extremities, or by their emotional expressions. Most people, however, have considered that these responses, generally called "startle responses," had to be evoked only by considerably intensive sounds, and would not appear for the weak sounds at the vicinity of the hearing threshold of the child. Moreover, they have believed that the intensities of the sound which elicit the responses were inconstant, varying according to the time and circumstances, even on the same examinee. It has been thus their common presumption that there was no strong relationship between the intensity of the sound which causes the responses and the hearing acuity of the examinee. Consequently, the testing procedure utilizing these reflex movements as the index of hearing has been regarded as a gross and informal one which could only indicate whether the examinee had the ability of hearing or not, and could not represent the degree of hearing loss in terms of threshold value. The sole reason why this informal test has so far been used often for the detection of the impaired hearing in the infant children is that there have been no other methods to test such small children without employing expensive equipment or a specially trained staff.

The most noteworthy study on the auditory measurement using this type of response was published in 1944 by I. R. Ewing and A. W. G. Ewing.[1] They tested 91 children with normal hearing, their ages ranging from one month to four years eleven months, and 170 infants suspected of deafness, using various kinds of sounds such as a) voice and speech; b) percussion toys including bell, drum, triangle,

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etc.; c) a range of pitchpipes from 120 cycles to 1900 cycles; d) "meaningful sound," e.g., chink of feeding bottle, knock at the door, light tapping, crackling or rustling of paper. They observed systematically and in detail their unspecific responses. The outline of the result of the test is as follows:

1) During the first three months of life, the infants with normal hearing responded to percussion sounds more quickly than to voice, and the manner of their response was reflex and took the form of blinking, screwing up of the eyes, involuntary jumping, etc. After four months old, however, infants met percussion sound with learned rather than with reflex response, and the voice steadily gained over the percussion sounds as a form of stimulation in winning quick response.

2) During the second half of the first year of life, learned responses replaced reflex reactions. For instance, they turned their eyes or faces toward the source of the sound and showed even their like or dislike of it by facial expression. The infants recognized the different complex sound, and voices attracted more and more their attention.

3) The sound of voice and speech proved more and more suitable as the testing sound as the children grew older, and moreover quiet speech was found to be more successful than loud speech in attracting their attention.

4) Children suspected of deafness retain more reflex reactions than those of normal hearing of the same age.

Similar testing procedure was described by Hughson and Thompson,[2] Froeschels,[3] Utley,[4] Wishart,[5] McLaurin,[6] and McHugh and McCoy.[7]

Of those testing techniques utilizing the startle responses as the index of hearing, the so-called "sound-field" or "free-field" test is most notable. In this procedure electrically controlled sounds are given to the examinee through a loud-speaker installed in a testing room. According to Myklebust,[8] "the sound-field test consists mainly of two types: pure tone and social sounds. The necessary equipment includes a beat frequency oscillator, an amplifier, a loud speaker and a turntable. Having two or more loud speakers is an advantage because it precludes the child's being more than a few feet from the source of sound at any one time although he might be moving about

the room. Moreover, switching the sounds from one speaker to another is useful as a testing procedure. As the child is seated at a table, the sounds are sent through the speaker at the intensities desired. The child might respond by looking up from his foreground activity and scanning his environment or he might respond more indirectly by momentary cessation of his activity." The author's opinion is that the sound-field test is an intermediary step between the more informal and more formal types of auditory testing and is useful chiefly for children between two and six years of age. He asserted that when peripheral deafness is present, the degree of the hearing loss can be explored with considerable assurance and accuracy by this method.

In 1954, Goodhill[9] modified this testing technique by adding a directional component to it, and named it "directional free field startle response audiometry." He used four matched speakers arranged in the four corners of the test cubicle of a two-room testing suite. It is thus possible to obtain additional information in a binaural free-field test by noting the accuracy of directional response, either by ocular or head movements on the part of the subject. Giving various social sounds such as noise makers, whistles, bells, drums, cymbals, etc., and switching them over from one speaker to another, the examinee was observed through an unidirectional window. However, as there is no testing result mentioned in the report of Goodhill, we cannot know how reliable and exact the test is.

In 1959, Hanaoka[10] attempted Goodhill's method on 48 infants not older than three years of age, considered to be of normal hearing, and found out that as much as 79.4 per cent of the total subjects had a threshold of under 30 db (average threshold of adults of normal hearing is 0 db). From this fact she pointed out that this method should be regarded as a quantitative method by which one could measure the hearing of infant children in decibel value. In the same year, Kanadani[11] also used the same method on 23 infants with severely impaired hearing, ranging in age from one year nine months to five years eleven months, and reported that the result obtained by this method was almost similar to that of GSR-audiometry or play audiometry.

The present paper deals with the investigation made by us in order to evaluate the reliability and validity of this type of audiometry as a quantitative method for measuring hearing acuity of children under three years of age.

EQUIPMENT AND PROCEDURE

On the ceiling of a sound-proof room, four small speakers are installed in such a position that they form a square of about 2 meters each side. These speakers are connected to a tape-recorder through push-buttons and an attenuator. Right underneath the square, at the middle, the infant to be examined shall be placed on the lap of an attendant sitting on a chair, the position of the infant's head being arranged so that the distance to each speaker is the same. It is of greatest importance not to let the child have any sort of fear or uneasiness. It is also necessary to instruct the attendant not to show any sort of interest in the test.

The sounds which we use in the test are the artificial sounds of cock's crowing, cow's mooing and cuckoo's singing, these being recorded on a tape in the following order:

(A)			(B)	(C)		(D)
10 sec.		10 sec.		10 sec.		
cock's	→	cow's	→	cuckoo's	→	cock's → cow's → cuckoo's
	2 sec.		2 sec.		3 sec.	

Sonagrams (section) of these sounds are shown in Figure 1.

The examiner should sit so that he can observe through an unidirectional window the expressions of the child, especially the movements of its eyes. Then a set of recorded sounds (i.e., from "A" to "B") is sent at an intensity level under the estimated threshold of the examinee. The testing room should be absolutely quiet when the test sounds are given to the child. Usually we present the initial sound stimulation through either of the front speakers. If there is any suspicion of hearing impairment in either ear of the child, the speaker at the side of the better ear is used. A set of testing sounds is followed by another with an increasing intensity of 10 db until some sign of responses is recognized. As soon as the response is recognized, the sound is switched to another speaker in order to evoke clearer responses by quickly changing the direction of the source of the sounds.

The responses observed in the examinee are to be summarized in the following six categories:

1. Movements of the eyeballs, or gazing at the source of the sounds.

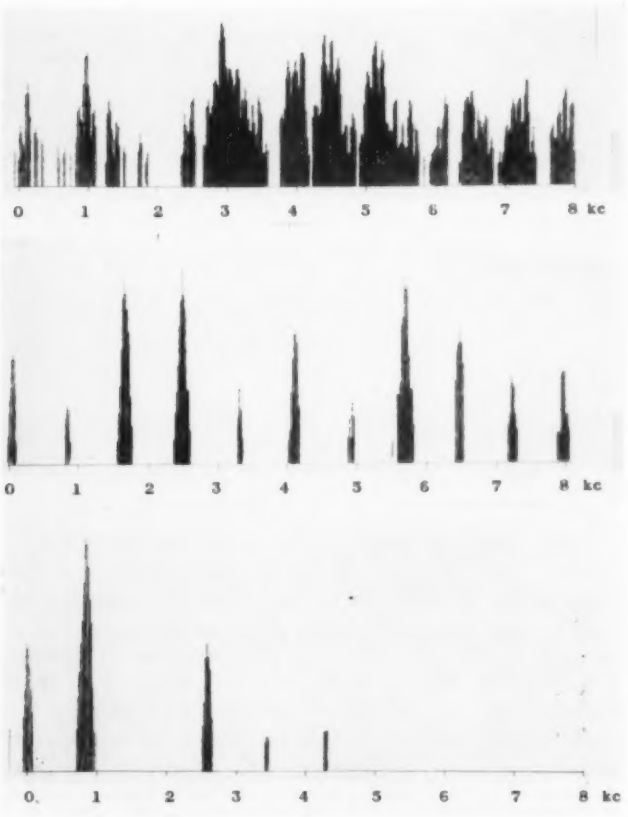

Fig. 1.—Sonagram (section) of test tones. Upper, "cow"; middle, "cock"; lower, "cuckoo."

2. Turning of the head toward the source of the sounds.

3. Ceasing of action.

4. Waking up from sleep.

5. Changes of expression (begins to smile or cry, or shows the surprise).

6. Responses by voice or speech.

TABLE I

DISTRIBUTION OF STARTLE RESPONSE THRESHOLDS AS A FUNCTION OF CHRONOLOGICAL AGE OF EXAMINEES

DB	~ 5 MO.	6 ~ 11 MO.	12 ~ 17 MO.	18 ~ 23 MO.	24 MO. ~
0			2	3	9
10		9	12	12	20
20	14	12	7	3	6
30	6	17	5	1	2
40	16	4	2	2	
50	10	1	1		
60	2	2			
70	1				
Total	49	45	29	21	37
Mean	36.5 db	26.0 db	18.6 db	13.8 db	10.2 db

RESULTS

Threshold of Responses on Normal Children. The threshold of the responses was measured on 181 consecutive infants and young children ranging in ages from 18 days to three years six months whose hearing was considered to be normal. The distribution of thresholds measured and their average value of each age class is shown in Table I. The result reveals the fact that the thresholds of responses of the examinees do not differ much from 0 db, approaching it gradually as the ages advance. In this table, 0 db means the average subjective threshold of adults when they hear the same sounds from the same source at the same position as the infant examinee. Accordingly, the results obtained seem to suggest the fact that the threshold of responses of the children thus measured would not be too far from their real hearing threshold.

In order to confirm this assumption, however, it is necessary to prove that the difference between the threshold measured by this testing procedure and that obtained by any subjective one is not significant. The above-mentioned 181 examinees being too young to determine their subjective threshold, another 38 children between the ages of four and nine years were selected for a comparison of both thresholds. Their thresholds of responses was first determined,

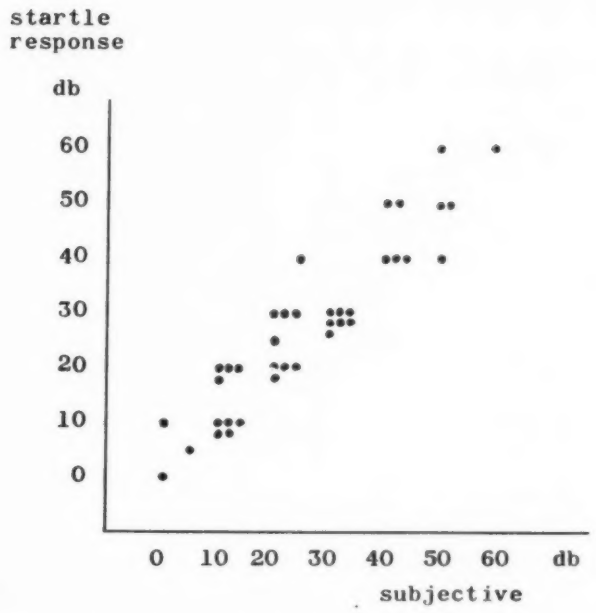

Fig. 2.—Comparison of the thresholds measured by startle response and by subjective method.

and then their subjective threshold was measured by using the same testing sounds and asking them whether they could hear the sounds or not. As is shown in Figure 2, in 24 out of 38 subjects or 63.2 per cent, both thresholds coincided with each other, the average difference being only 3.2 db.

Kinds of Responses and Frequency of Their Appearances. Kinds of the responses of the above-mentioned 181 children are shown in Table II. As the responses made more than twice by the same child were counted separately, the total number of the responses have been entered as 271.

The most frequently appearing responses are Nos. 1 and 2, both being made by about half of the 181 children tested. An interesting fact is that the children under the age of one year responded mostly with movement of the eyes, whereas the children older than one year

TABLE II

KINDS OF THE RESPONSES AND ITS INCIDENCE

RESPONSES	~ 5 MO.	6 ~ 11 MO.	12 ~ 23 MO.	24 MO. ~	TOTAL
1. Movements of the eyeballs	34	28	15	15	92
2. Turning of the head	16	22	35	25	98
3. Ceasing of action	4	4	2	2	12
4. Waking up from sleep	3	1	1	0	5
5. Changes of expressions	8	14	11	9	42
6. Responses by voice or speech	4	1	12	5	22
Total	69	70	76	56	271

responded rather by turning their head. Other responses did not appear so frequently as No. 1 or 2 and were found to be mostly accompanied by either No. 1 or 2.

Comparison with the Pure Tone Audiometry. Table III demonstrates the comparison of the thresholds of the responses with those measured by the pure tone audiometry. The examinees entered in Table III include children with normal hearing and those considered to have severely impaired ears. The pure tone thresholds which are mentioned in the right column of the table are determined by using the testing procedure of the play audiometry or the conditioned orientation reflex audiometry (COR-audiometry)[12,13] according to the age of the examinees.

By comparing both thresholds, startle response and pure tone, we find that both are considerably near each other. This is also a fact which affords a proof of the startle response audiometry being a useful tool for measuring the hearing impairment quantitatively.

COMMENT

As for testing sounds, we have been using animal sounds so far, but we are not saying that they are the best. Any kind of social

TABLE III

COMPARISON OF STARTLE RESPONSE AND PURE TONE AUDIOMETRY

AGE	STARTLE RESPONSE AUDIOMETRY		PURE TONE AUDIOMETRY 500	1000	2000	4000 CPS	METHOD
0: 8	25 db		45 db	45 db	40 db	50 dL	COR
0:11	70↓		70↓	80↓	80↓	80↓	COR
1: 2	15		15	15	10	5	COR
1: 3	10		20	15	10	15	COR
1: 4	10		25	20	20	20	COR
1: 7	0		15	10	10	15	COR
1:11	10		15	10	10	10	COR
2: 1	50		25	30	40	35	COR
2: 1	60		65	80	75	75	COR
2: 1	70↓		70↓	80↓	80↓	80↓	COR
2: 3	5		15	10	10	15	COR
2: 4	50		45	55	55	55	COR
2: 5	5		15	10	10	5	COR
2: 7	10		15	10	10	10	COR
2: 8	70↓		70↓	80↓	80↓	80↓	COR
2:10	40		50	65	70	80	COR
2:10	0		15	10	10	15	COR
3: 7	40	L.	35	60	80↓	75↓	Play
		R.	45	75	80↓	75↓	
4: 0	60	L.	40	35	35	45	Play
		R.	45	40	40	40	
4:10	20	L.	20	20	10	15	Play
		R.	40	30	20	35	
5: 0	60	L.	65	55	60	60	Play
		R.	60	60	65	55	
9: 3	50	L.	60	50	45	55	Play
		R.	55	50	50	45	

sounds which attract the children's attention will get the same result. However, to use too many kinds of sound will only make the test complicated. Pure tone or musical sound which is near to pure tone is not suitable for a testing sound since it does not startle the children to a great extent. It is true that pure tone can also cause the startle responses, but it will have to be at the intensity level of test tone much higher than that of any social sounds in order to effect startle responses.

Checking and rechecking many sort of responses of the examinees, the most important responses were found to be the movements of the eyes and the turning of the head. However, attention must be called to the fact that these responses being to appear, as is described by Ewing and Ewing, in infants after they are three months old, and it would be inadequate to use the responses above-mentioned as the indicator of hearing of infants younger than three months old.

The principle of this method is rather a primitive one and has so far been applied only to find out whether the child could hear or not. Present observation, however, has made it clear that such an opinion was a prejudice, because these startle responses appeared almost always at the intensity level of sounds very close to the subjective threshold of the examinees.

Chief handicaps of this method are: 1) being administered in a free field, it cannot test the hearing of each ear separately; 2) testing by the use of pure tone is difficult though not impossible; 3) especially for older children, it is difficult to follow up the change of hearing by a series of testing, since the responses do not appear so clearly at repeated tests as at the first test.

SUMMARY

A modified testing procedure utilizing the auditory startle response as the index of hearing is described. Four speakers are equipped at the four corners of the testing cubicle, and the artificial animal sounds are used as the test sounds. Most important responses observed in the examinee are found to be 1) movements of the eyeballs and 2) turning of the head toward the source of the auditory stimulation. The responses are evoked at the intensity level of the sound very close to the subjective threshold of the examinee, the average difference between both thresholds being only 3.2 db.

The authors believe that startle response audiometry is a reliable means of measuring the degree of auditory impairment expressed in threshold value for infants above three months of age.

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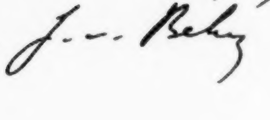

THE NOBEL PRIZE IN MEDICINE

* * *

GEORGE VON BÉKÉSY

* * *

On October 19, 1961, almost everyone, it seemed, knew who the recipient of the 1960 Nobel prize in Medicine was, except the recipient himself. The news came over the radio and television early in the morning, but up till noontime on that day, the news had not reached Dr. George von Békésy. He had left Boston two days earlier, and being a bachelor, had left no forwarding address. Hence, nobody had been able to contact him on the morning of the exciting news. He learned of the award as he came into the Waldorf Astoria Hotel to receive a gold medal award from the Deafness Research Foundation, and it took him completely by surprise.

It is interesting to note that Dr. von Békésy considers himself a physicist, yet he has won the Nobel prize in medicine.

George von Békésy was born in Budapest, Hungary on June 3, 1899. He graduated from the University of Berne in 1920 and earned a Ph.D. from the University of Budapest in 1923. He immediately went to work for the Hungarian Telephone system and through the study of telephone communications, became interested in the subject of hearing. Thus began a lifetime of study of the functions of the ear. He remained in Hungary until 1946, when he studied at the Karolinska Institute in Stockholm, Sweden and there became a research professor in 1947. He came to the United States that year and was research lecturer in the Psycho-Acoustic laboratory for two years, then earned the title of Senior Research Fellow in psychophysics at Harvard. He has remained in that position ever since.

Through meticulous study with the use of the microscope, he has investigated the functions of the inner ear. Perhaps his greatest discovery is the fact that he found that different pitches did not excite different fibers of the basilar membrane, as was previously thought. He found, through detailed study, that vibrations went

along the basilar membrane to a point where there was a maximum amplitude and the maximum amplitude occurred, he found, at the same point on the basilar membrane when the same pitch was used.

He is continuing his studies on the ear and feels that there is much yet to be learned. He is presently doing some studies on skin sensations, because he feels that some of the reactions of the skin are similar to those of the ear.

Dr. von Békésy has been awarded ten special awards or gold medals during his lifetime and amongst these are the gold medals of the American Otological Society, the American Acoustical Society and the Deafness Research Foundation.

It is of interest to all physicians that this researcher in physics has been awarded two honorary doctorates of medicine, one from the University of Berne and one from the University of Wilhelm in Muenster, Germany. He is one of the few physicists who have been awarded the Nobel prize in Medicine. Roentgen was one of his notable predecessors.

HOOPLE

LXXIII

MODIFICATION OF MYERSON'S TECHNIQUE IN THE MOBILIZATION OF THE STAPES

JUAN ANDRADE PRADILLO, M.D.

MEXICO, D. F.

As we all know, we owe to Rosen the introduction of stapes mobilization into therapeutic surgery to restore hearing in otosclerosis. This is an important advance in spite of our ignorance of the etiology and pathogenesis of the disease. Various authors have employed new methods consisting of indirect mobilization, direct mobilization and fenestration of the oval window.[1,2]

In July of 1957 I decided to employ Myerson's technique in my service at the General Hospital of México City. This technique as is well understood consists in applying a vibratory impulse through the ossicular chain starting with the short process of the malleus by means of a fork-shaped instrument which is plâced firmly over it.

A flattened rod is rotated at 9000 r.p.m. and brought into contact with the body of the fork, thereby generating vibrations which progress along the fork to the short process of the malleus, to the ossicular chain and the foot of the stapes.[3]

When I tried to locate the fork over the short process of the malleus it slipped toward the back, then forward and again to a position high in the rear, bearing accidentally on the neck of the malleus. In this somewhat unorthodox position I was able to apply the vibratory stimulus and after 15 minutes the patient was able to hear a whispered voice. In view of these encouraging results I operated on the other ear a week after with the same good results. I am informed that the patient has retained good hearing after three years. Similar experiences occurred with other patients and I decided to modify the technique by perforating Schrapnell's membrane and bearing on the neck, a modification which I have continued to practice.

Before attempting to describe the technique, it would seem important to review some aspects of the anatomy.[4] Through the specu-

lum we can see the short process of the malleus located high and forward. A white strip, wider in its upper half, can be seen descending from there: the handle of the malleus. The axis of the head does not follow the same direction as the handle. At the height of the neck it forms an angle of about 140°. This is not the angle that is apparent since the head is directed upwards towards the rear and inwards so that the angle in relation to the plane of the membrane is slightly larger (150°). We will see later that this direction is important.

TECHNIQUE OF THE OPERATION

The preparation and local anesthesia are well known. A microscope or magnifying glasses can be used. In one case I had to use a headlight without magnification.

INSTRUMENTS

Ear specula.

Hartmann forceps.

Rosen aspirator tube.

Fork instrument consisting of a handle and a 7 cm long flattened shaft 2.5 mm thick. The end of the shaft is shaped like a fork with a depth of .5 mm to permit its location on the neck of the malleus. The shaft is curved slightly downwards, and it must be made of tempered steel and flexible as a clock spring.

A cylindrical rod about 6 mm in diameter with one side tapering, flattened at one end, resembling a chisel in shape but only on one side of the rod (Fig. 2). The rod is connected to a dental hand-piece to apply a rotatory motion.

An otometer.

Position of the Patient. Dorsal decubitus for the right side and ventral decubitus for left side with the head turned left.

Position of the Surgeon and Assistant. The surgeon stands on the left side and the assistant sits in front of him. They must be comfortable and well relaxed to prevent fatigue since once the vibration is begun they must remain in the same position throughout the application at the risk of failure. The technique is very simple but it must be applied perfectly.

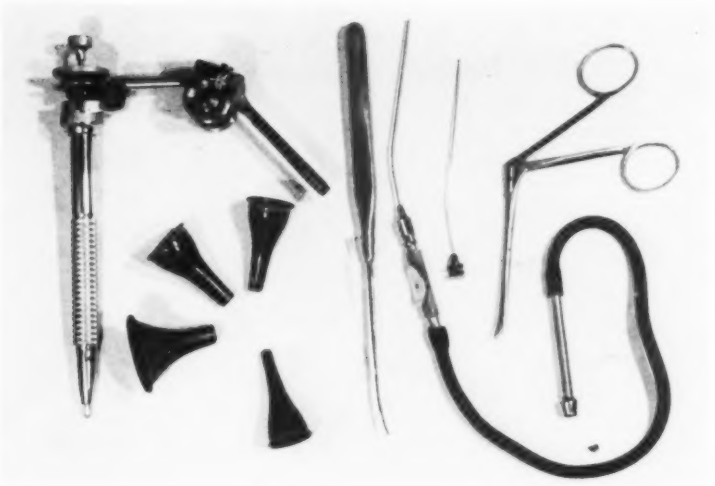

Fig. 1.—Instruments.

Location of the Short Process of the Malleus. Sometimes after the application of the upper injection an edema occurs which obliterates it. Then it should be located by feel with the use of the aspirator tube.

Placement of the Fork. The handle of the instrument is grasped like a pen with the concave side downwards. The membrane is perforated immediately behind and above the short process of the malleus until the fork rests on the neck (Fig. 3). The contact should be made without exerting force but rather using the weight of the hand and forearm on the instrument without touching the patient. This will result in a force on the instrument of approximately 300 grams. This force results when the instrument is being grasped and does not correspond to the force resulting from a complete relaxation of the hand and forearm which would increase over 800 grams.

Contact of the Flattened Rod. The assistant must take the handle of the dental hand-piece as he would a pen and should make gentle but firm contact between the rod and the underside of the fork about 2 cm outside the speculum. It is convenient to rest the right hand on the left hand which in turn should rest on the face of the patient.

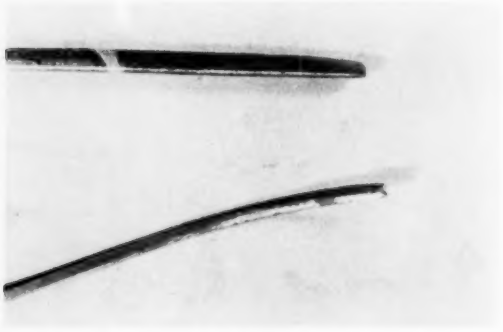

Fig. 2.—Cylindrical flattened rod and fork.

In this manner even if the assistant should push unduly the fork will not disengage since it would bear against the outer attic wall.

Vibration. The vibration generated by the flattened rod will, of course, be damped by the flexibility of the fork body. It should be initiated mildly by contacting the rod at the point where the flat begins in the shape of a "V". The strength of the vibration will be increased at the request of the surgeon by displacing the flattened rod towards its tips where the flat is almost as deep as half the diameter of the rod. The number of revolutions per minute should be as high as possible from the beginning, since the time of the operation will diminish as the frequency of vibrations increases.

It is absolutely necessary that the patient remain motionless during the entire operation and he be warned to advise the surgeon in case motion becomes imperative and then the motor should be stopped and the fork removed. The application should be repeated if the time elapsed was under five minutes. After 15 minutes of application the operation should stop in order to perform tests especially with the voice.

I have found that inexact data may be obtained by the use of the audiometer because the patient is apt to be confused due to the intense noise experienced during the operation. If the patient has recovered audition the operation should be stopped but if the improvement is not enough, vibration for another 15 minutes should be applied after three minutes' rest.

I have had cases in which positive results were obtained in this second session. I have come to the conclusion that if results are negative after 30 minutes' application it is useless to continue. Postoperative care is the same as for any mobilization.

ABSTRACT OF CASES OBSERVED

Number of cases	76
Ages 15 to 30 years	22
30 to 50 years	26
50 or more	28
Otosclerosis	48
Misc. Deafness	28
Degree of Deafness	
Light (20-40 db)	2
Moderate (40-60 db)	43
Marked (60-80 db)	21
Acute (80 or more)	10
Immediate Postoperative Results	
Excellent	30
Good	41
No improvement	5
Condition worse	0
Results 2 Years After the Operation	
Excellent	7
Good	15
Satisfactory for the patient	8
Improvement lost after 2 months	23
Unknown	23

COMPLICATIONS

In one case the perforation did not heal by itself after one month, but it did after the application of trichloracetic acid.

In one case there was a moderate otitis which disappeared. In five cases there was temporary vertigo.

COMMENT

In 71 cases definitive improvement was observed immediately after the operation. In some cases the patient could hear not only the normal whispered voice but a voice in a very low whisper. Many retained the improvement for a few hours, others for days, still others for months and some two years after the operation. Eight cases are

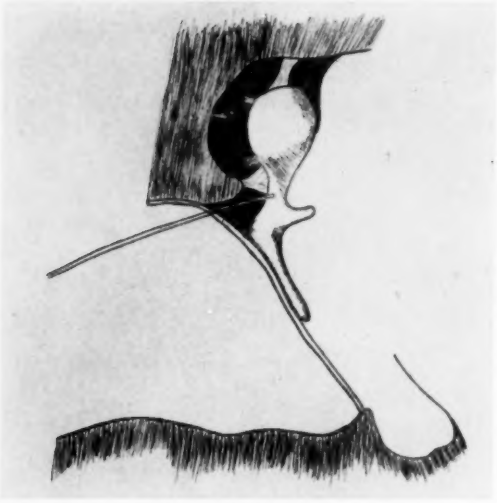

Fig. 3.—The fork perforates Shrapnell's membrane and rests on the neck of the malleus.

shown as satisfactory for the patient because even though audiometry showed no improvement the patients insist that they hear better. In five cases there was temporary vertigo lasting from a few hours to several days and this effect seems to correspond with a lasting improvement in hearing.

It is interesting to discuss some of the cases that are peculiar in some respects in order to complement the data already shown.

CASE 1. Man 46 years old. Hypertension. No deafness in family. Slowly developed deafness. (Negative Rinne in both ears.) Intelligibility 70%. (Tinnitus)

Right Ear	June 20, 1957	70	45	48	60
	bone	10	0	20	28
	June 22, 1957	operated upon			
	June 27, 1957	45	25	30	33
	July 10, 1957	10	10	20	23
	Sept. 25, 1957	0	0	3	3

After 2 years he kept on hearing well. This was the first case in which I accidentally applied vibrations to the neck. After 15 minutes of treatment he was able to hear a whispered voice. He had vertigo for three days.

Left Ear	June 20, 1957	55	30	35	40
	bone	8	0	10	28
	June 29, 1957	operation			
	July 3, 1957	45	25	35	38
	Aug. 10, 1957	10	10	10	30
	Sept. 25, 1957	0	0	2	

After 2 years he kept on hearing well. He was given 15 minutes of treatment, being able to hear a whispered voice. He had vertigo for one day. The tinnitus disappeared on both sides.

Comment. This case can be considered as excellent in results.

CASE 2. Thirty years of age. Negative Rinne in both ears. Slowly increasing deafness. Intelligibility 97%.

Right Ear	May, 20, 1959	50	50	45	50	45
	bone	0	15	25	15	
	May 25, 1959	operation				
	July 23, 1959	20	25	28	15	
	Aug. 6, 1960	8	10	4	15	

I have been informed that her condition has suffered no appreciable change until the present time. After 15 minutes' vibration treatment she could hear vowels in a low whisper.

Left Ear	June 10, 1959	40	35	40	35
	bone	10	10	5	35
	June 13, 1959	operation			
	June 23, 1959	22	23	28	20
	July 23, 1959	18	23	25	10
	Aug. 6, 1960	25	35	25	10

After 20 minutes' treatment she could hear whispered voice.

Comment. This is a case of a young women in perfect health. The results may be considered good.

CASE 3. Male, 15 years of age, with a history of amygdalitis and adenoiditis. Slowly increasing deafness. Negative Rinne in both ears. Bing position in both. 80% perception.

Left Ear	May 8, 1957		50	50	60	40
		bone	5	8	0	20
	July 6, 1957		operation			
	Aug. 6, 1957		42	40	30	23

The patient did not return for observation. After 15 minutes' treatment he could hear a normal voice.

Right Ear	May 8, 1957		55	55	55	60	60
		bone	10	8	10	5	
	July 13, 1957		operation				
	Aug. 6, 1957		40	40	20	20	
	Aug. 17, 1957		15	10	10	8	

The patient did not return for observation. After 12 minutes' vibration he could hear a normal voice.

Comment. The present condition of this patient is not known.

CASE 4. Woman, 51 years of age. Married with several healthy children. No family deafness. Arterial hypertension. Negative Rinne in both ears. 90% perception. Wearing hearing aid in the right ear.

Right Ear	Nov. 7, 1957		60	55	53	48
		bone	0	3	5	8
	Nov. 12, 1957		operation			
	Nov. 30, 1957		5	5	10	15
	Jan. 8, 1958		4	5	10	18
	Nov. 8, 1960		48	53	35	38

After three minutes' vibration she felt her ear unplugging and after seven minutes she could hear vowels in a low whisper. In view of the worsening of her audition in Nov. 1960 she accepted a second mobilization in the same ear. She felt this condition was owing to a series of upsets and to the fact that her blood pressure increased to 240. On the 19th of December, 1960, she was operated upon again and after 15 minutes' treatment she could hear a whispered voice.

	Dec. 23, 1960	20	30	28	30
	Jan. 12, 1961	5	10	23	30
Left Ear	Nov. 7, 1957	53	45	40	30
	Dec. 6, 1957	operation			
	Jan. 23, 1959	20	20	10	15
	Nov. 8, 1960	30	35	20	15

After 15 minutes' vibration she could hear a whispered voice.

Comment. This is a case in which the good results of a second operation on the same ear are demonstrated. The right ear also showed by Nov. 1960 a decrease in hearing relative to the excellent results of the operation. This may have been caused by the serious psychological and circulatory disturbances to which the patient was subjected. This case I classifiy among the excellent ones; the patient has not used a hearing aid since the operation. This good result may be conserved very likely, by watchful care of her general health.

CASE 5. Man, 71 years of age. Has had cardiac infarct, extreme deafness since early age. A person of perennial good humor. He uses a hearing aid in the left ear in which he has chronic otitis. In the right ear the deafness was so pronounced that when the hearing aid was out of order people would have to communicate with him through writing.

Right Ear	Jan. 30, 1958	70	80	85	84
	bone	0	10	23	35
	Rinne negative. Gelle position.				
	Feb. 10, 1958	Operation			
	Feb. 14, 1958	77	70	75	70

He could hear a loud voice at close range after 45 minutes' treatment. To this date his condition is exactly the same in spite of having suffered a new infarct.

Comment. This is a case where the improvement is rather modest but the patient is very well satisfied with the results. It has been impossible to convince him that he should use a hearing aid in the right ear.

CASE 6. Woman, single, 27 years of age. Rapid deafness in recent years. Rinne negative. Bing position on both sides. 75% perception. Uses a hearing aid on both sides.

Right Ear	Oct. 25, 1957	70	70	70	80	95
	bone	5	5	15	40	
	Nov. 11, 1957	operated				
	Mar. 6, 1958	60	50	58	65	
	Jan. 23, 1959	70	70	63	80	
	Jan. 28, 1959	Another mobilization was performed but there was no improvement immediately after the operation.				
Left Ear	Oct. 25, 1957	63	63	63	70	85
	bone	5	5	10	40	

After 18 minutes' application she improved slightly but after some days she lost all that had been gained. In the right ear the paracentesis did not heal in the course of one month and it was necessary to apply trichloracetic acid. She was given 2 mg of cortisone for one month appearing to gain temporary improvement. The patient is again using a hearing aid.

Comment. No positive or negative results were obtained in this case.

CASE 7. Woman, single, 39 years of age, 90% perception. Rinne negative. Uses a hearing aid on the left side.

Right Ear	Sept. 24, 1957	70	70	70	60	50
	bone	5	0	15	25	35
	Sept. 26, 1957	operation				
	Sept. 30, 1957	25	15	20	25	40
	Oct. 21, 1957	15	20	12	10	15
	Oct. 30, 1957	12	5	0	10	30
	Aug. 27, 1960	48	45	58	65	

After 10 minutes' vibration she could hear a whispered voice. She had vertigo and nystagmus and headache for two days.

Left Ear	Sept. 24, 1957	60	50	50	40	35
	bone	5	0	8	15	15
	Oct. 10, 1957	Operation				
	Oct. 17, 1957	40	40	23	18	15
	June 3, 1958	40	30	28	45	
	Aug. 27, 1960	58	58	50	58	

She felt vertigo when the injection was being applied. After 10 minutes' vibration she was able to hear a whispered voice. Headache that afternoon. The patient is back to using a hearing aid in the left ear.

Comment. This case shows very good, but temporary, improvement. The net result has been a psychological prostration of the patient who, having enjoyed a marked improvement, had to revert to the use of a hearing aid. Something to be noted is that the condition of the ear in which the patient uses the hearing aid has kept on deteriorating whereas the other ear has suffered no further hearing loss. This case tends to confirm the importance of re-education. There is a factually proven improvement in the right ear after three years.

GENERAL COMMENT

Upon review of the various cases it can be observed that in no case was there a worsening of the condition; there were no complications. The immediate results were truly satisfactory but the percentage of definite results was considerably lower. As mentioned, I have been unable to gather reports on 23 cases out of 76 patients operated upon but of the 53, 30 may be considered successful and 23 unsuccessful (no improvement gained) which would indicate 51 to 58% successful cases.

The fact that a patient may gain substantial improvement with the operation, only to relapse gradually, is disappointing. There was a case in which a man suffering from extreme deafness and not being able to use a hearing aid was operated upon. Results were so good that against all advice he left, driving his automobile, and later when with some of his friends had been completely able to enjoy a conver-

sation. However his disappointment the next day was tremendous after reverting to his previous condition, in spite of having been advised of this possibility.

Wullstein considers that a really deaf patient will be very happy to attain a degree of improvement. It is necessary to discard the idea that a success can be considered when only the 30 db hearing loss is reached. Patients with a slight perception loss are the most demanding especially if there are other cases of deafness in their families.

The evolution of deafness is a very important factor. There are some cases which remain latent for years and suddenly start on a course of rapid deterioration. This is the time when the patient demands a cure from the surgeon. It is of no use to attempt to correct the lesion since the basic cause is unknown. We may obtain an immediate success but, since the cause persists, will ultimately fail in spite of a good technique.

The various cases must be resolved in manners indicated by peculiar conditions.

It is impossible in this paper to attempt to consider cases like deafness with red membrane, old otitis with modification of the ossicular chain and trauma resulting from boxing or other causes.

I believe, as many authors do, that a simple technique should not be discarded especially if there is no worsening of the condition and no impediment against repeated interventions in case of failure. The only drawback seems to the psychic disappointment of the patient who opposes new surgical interventions. In this type of surgery the truly humane and able physician must place the patient in a proper mental condition to accept a second operation should the first one fail.

CONCLUSIONS

The procedure is innocuous. No complications arise. In no patient did the condition worsen. Re-ankylosis occurred in numerous cases. It would be very good to be able to retain the immediate success. Present research is directed towards this goal.

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LXXIV

THE ELECTRICAL POLARIZATION OF THE SEMICIRCULAR CANALS (GUINEA PIG)*

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The endolymph in the scala media of the cochlea of a guinea pig shows a resting electrical potential of about +80 mv relative to the perilymph in scala tympani or scala vestibuli.[1,2,10] On the other hand the potential of the endolymph in the utricle and saccule is not more than +5 mv.[7] Dr. I. Tasaki has confirmed this observatoin (personal communication). At first sight it is difficult to reconcile this low potential in the saccule with the high potential in scala media, but Misrahy[6] has shown that the values are compatible because the ductus reuniens, which unites the structures, is very narrow, as shown in Figure 4, and its walls are electrically leaky. Recently Trincker[14-17] has reported that the endolymph in the lateral semicircular canal of the guinea pig is 30 to 40 mv positive relative to the perilymph. The semicircular canals, however, open directly into the utricle and a potential difference of more than a very few millivolts between them seems implausible if not impossible. We have therefore undertaken to verify Trincker's electrical measurements in the ampulla.

METHOD

Guinea pigs were anesthetized with Dial® in urethane, 0.50 cc per kilo of body weight injected intraperitoneally. We employed a postero-lateral approach, entering the middle ear cavity and exposing the ampulla of the posterior semicircular canal. In some experiments the membranous labyrinth was widely exposed to obtain as clear a view as possible of the crista within the ampulla. In most experiments the opening in the bony wall was deliberately kept small in order to minimize the possibility of mechanical disturbance of the structures within

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and to reduce the escape of perilymph. The position of the animal's head and the opening into the bone were such that perilymph always covered the membranous labyrinth. In four experiments the lateral ampulla was exposed, by first opening the canal of the facial nerve close to the stapes.

Our microelectrodes were glass capillaries filled with 3-molar KCl.[10,12] Their resistance was between five and ten megohms. The resistance of the microelectrode was always measured immediately before use, with its tip dipping into an isotonic solution of sodium chloride, and only electrodes that showed values between five and ten megohms were employed. The tips were less than 1 μ outside diameter. The taper was about 1:10 for a short distance back from the tip but then became very gradual until a diameter of about 20 μ was reached at a millimeter from the tip. This gradual taper allowed deep penetration through the wall of the membranous labyrinth with a minimum of injury.

The microelectrode was attached to a lucite carrier which was mounted in turn on a micromanipulator (Emerson). In order to record the forward movement of the microelectrode, a hydraulic indicator system was connected to the micromanipulator. A metal arm clamped to the electrode carrier moved the plunger of a 10 cc glass syringe. The syringe was connected flexibly to a small glass tube mounted horizontally immediately above the oscilloscope. The position of the fluid meniscus in this tube indicated the position of the tip of the microelectrode. The hydraulic amplification of its forward movement was about x 100. In order to photograph the position of the meniscus on moving film (Grass camera) it was "tracked" by hand, in some experiments, with a small incandescent electric light bulb. In other experiments, still pictures were taken of the meniscus, its scale, and the oscilloscope after each change in potential indicated by the latter. This method gave more accurate indication of the position of the tip of the microelectrode than the method of tracking the meniscus with a hand-held light but it did not record the details of the potential changes as the electrode entered or emerged from individual cells.

Electrical contact with the potassium chloride solution in the microelectrode was made with a freshly chlorided silver wire that was inserted directly into the large end of the micropipette. The other end of the wire led directly to the grid cap of the first (cathode follower) stage of a DC amplifier. It was a differential amplifier, but the grid cap of the second input tube was grounded. The circuit was

completed to the animal through another chlorided silver wire. In early experiments the wire was simply wrapped in cotton moistened with isotonic NaCl solution. In later experiments it was inserted into a wide-bore glass tube filled with 3-molar KCl solution and contact with the exposed tissues at the edge of the operative wound was made through a plug of agar jelly made with isotonic NaCl solution. Thus when the tip of the microelectrode dipped into the perilymph outside the membranous labyrinth, the electrode system was very nearly symmetrical. The large electrode also served to ground the animal.

The DC amplifier was the same one that has been used in our laboratory for several years.[10,11] The input (cathode follower) tubes were RCA 1620 connected in triode. Their grid current with a micropipette was approximately 4×10^{-11} amp.[9]

The reference potential was that of the perilymph just outside the membranous wall of the posterior semicircular canal close to the ampulla. The electrode was slowly advanced through the wall toward the crista or the cupula while the DC potential and the position of the electrode were recorded photographically as described above.

RESULTS

As the microelectrode penetrated the wall of the membranous labyrinth it registered irregular negative potentials of 20 to as much as 50 or sometimes even 70 mv, presumably from the interiors of the cells that compose the membranous wall.[1,2,14,15] The registration of these intracellular potentials was evidence that the electrode had actually entered the wall. Sometimes an indentation of the wall could be observed under the dissecting microscope, sometimes it could not. Following a slight further advance the measured potential rose abruptly to very nearly its original level. The electrode was then advanced to a total depth of 1.5 to 2.0 mm or else until the tip was broken by encountering bone. Breakage of the tip usually caused a sudden positive shift of potential of a few millivolts which was maintained when the electrode was withdrawn to the perilymph. The positive shift was apparently due to the fall in input resistance caused by the breaking of the tip. It was very small in the later experiments of the series when particular care had been taken to make the electrode system symmetrical by inserting the ground wire into 3-molar KCl solution and connecting it to the animal by a bridge of agar jelly made with isotonic NaCl. The tip of the microelectrode was examined under a microscope after withdrawal to verify suspected breakages of the tip and the input impedance was measured again. No experi-

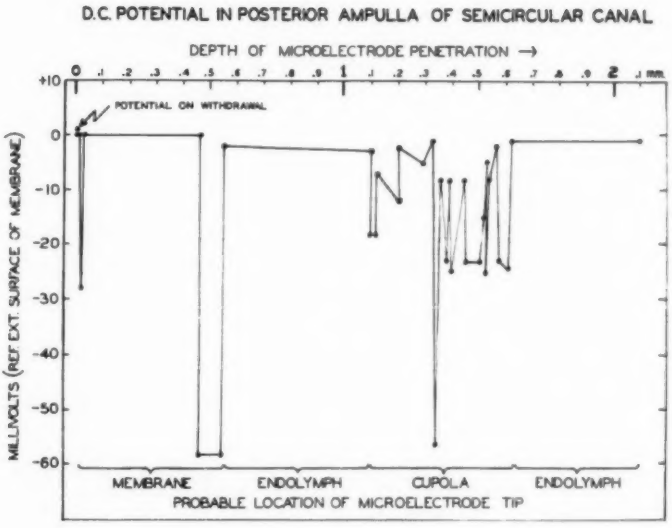

Fig. 1.—Graph of electrical potential differences relative to the perilymph just outside the membranous labyrinth as a function of the forward movement of the tip of the microelectrode. The potential and the position were both recorded continuously on moving film, using the method of "tracking" by hand the movements of a fluid meniscus as described in the text. The tip of the electrode was unbroken on withdrawal. The interpretation, given below the graph, that the electrode passed through the cupula rather than the crista is based on microdissection made after five penetrations at slightly different levels.

ment was considered satisfactory unless the potential recorded in the perilymph outside the membranous labyrinth was within 5 millivolts of the initial reference zero. Larger differeneces were always associated with broken tips or tips that appeared obstructed by bits of cellular material. With broken or obstructed tips there was always a change in electrical resistance, but when the potential of the perilymph was within 5 mv of the initial reference level breakage or obstruction of the tips of electrodes were never observed.

Eight preliminary experiments were performed with electrodes about 3 μ diameter. The results were perfectly consistent with those of the more satisfactory experiments with electrodes of 1 μ or less in diameter. Two additional preliminary experiments were performed with the smaller electrodes.

In the final series, a total of 18 technically satisfactory penetrations of the ampulla of the posterior semicircular canal were made in five animals. A total of 16 penertations in 4 animals were made into the ampulla of the lateral semicircular canal. The penetrations were made at various levels and at various angles relative to the crista. At a depth corresponding to the expected position of the crista strong negative potentials, from —30 to —70 mv, were regularly encountered. These were presumably intracellular potentials.

Figure 1 shows the potential measured at various depths in one of the satisfactory penetrations. The numerical values of potential and position were read from the photographic film. They include all of the maxima and minima that were recorded. The points are joined by arbitrary straight lines. The potential changes indicated on the film were typically abrupt and the plateaus were well maintained, as indicated. Where slanting lines are drawn, the potential changes were either gradual or irregular.

In no experiment did we ever encounter the positive endolymphatic potential of +20 to +40 mv described by Trincker.[14,15] The value measured just inside the wall of the semicircular canal was —1.0 mv. Because of a tendency of our zero base line to drift very slightly negative, this value is not significantly different from zero. The most positive value measured in any technically satisfactory situation was +4 mv, measured deep in the ampulla during withdrawal of the pipette. We never encountered positive potentials in the region of the cupula where Trincker[14,15] reports potentials as high as +70 mv.

If there was any question about the position of our electrode microdissection of the ampulla was done immediately after the experiment. As an additional control on the position of the tip of our exploring electrodes in one experiment, the temporal bone was fixed by intravital perfusion with Heidenhain-Susa solution and was ultimately examined in serial sections under the microscope. The point of entry of the microelectrode through the wall of the membranous labyrinth was readily identified and also the track of the electrode through the crista as indicated in the drawings (Figs. 2 and 3). The micropipette is indicated diagramatically in Figure 2. The results of the histological study in this animal agreed so closely with the direct observations made with the dissecting microscope during the experiment and recorded at the time that further controls of this sort were deemed unnecessary. In many experiments the crista could be identified quite clearly through the wall of the membranous labyrinth and the electrode aimed accordingly. It will be recalled that the diameter

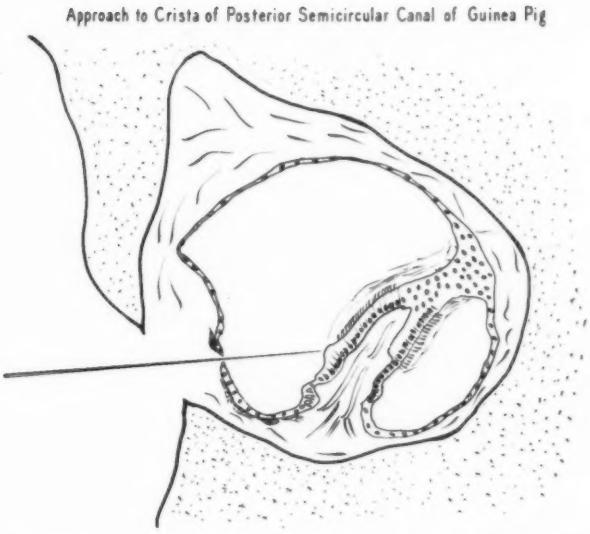

Fig. 2.—Camera lucida drawing of the posterior semicircular canal of guinea pig showing the fenestra through the bone and the hole through the wall of the membranous labyrinth. The electrode is drawn diagramatically, approximately to scale, although the section was not made in the plane of the electrode track.

of the micropipette was about 20 μ at a distance of 1 mm from the tip, and on account of fixation artefacts it would have been impossible to identify with certainty any microelectrode tracks in the cupula.

Although penetration of the cupula without entering cells of the crista could not be proved completely in any particular penetration it seemed certain, on subsequent microdissection, that many of the negative potentials must have been recorded while the tip was in the cupula and not within the cells of the crista. There is no doubt, however, that the potentials everywhere within the ampulla were always either negative or practically zero.

As an additional control in this series of experiments, as in our previous series,[7] we have several times inserted a microelectrode both into the cochlear duct (scala media) and also into the utricle or an ampulla in the same animal. In every case the high positive potential of the scala media was successfully recorded but no potentials greater

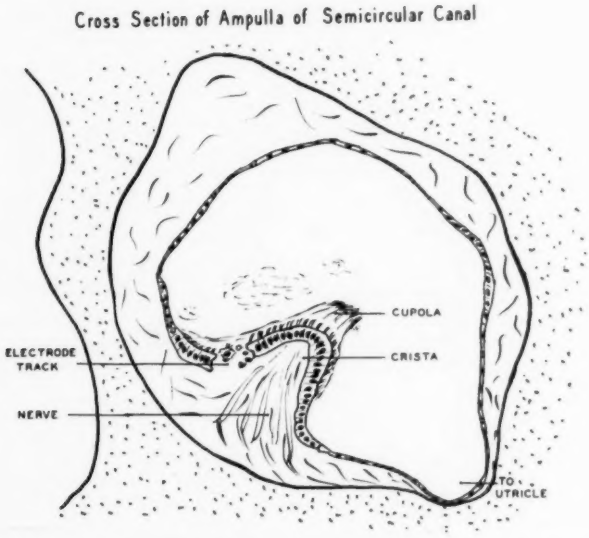

Fig. 3.—Drawing of another section of same specimen as in Figure 2, showing the electrode track passing through the cells of the crista. The electrode was introduced deeply and its relatively large shank destroyed some of the cells.

than about 5 millivolts were ever recorded from any other region. Our best estimates of the DC potentials in the membranous labyrinth are summarized in Figure 4.

COMMENT

Our measurements of DC potential in the membranous labyrinth form a self-consistent set in which the high positive potential appears only in the scala media of the cochlea. The source of this positive potential has been identified as the stria vascularis.[3,13] It is worth noting that within the scala media neither we nor Békésy have found any potential gradients within the endolymph. (The diagram given by Davis, Tasaki and Goldstein[4] was based on an erroneous extrapolation before direct measurements had been made with microelectrodes.) There is no structure in the non-auditory portion of the labyrinth that corresponds closely to the stria vascularis. The high positive potential appears to be correlated strictly with the stria vascularis, and the difference of potential between the scala media and the saccule is

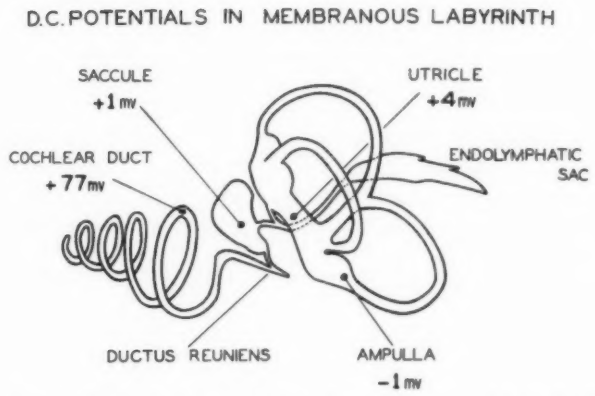

Fig. 4.—The electrical polarization of the membranous labyrinth of the guinea pig. The values are the most representative of our measurements in technically satisfactory trials in the present and previous experiments.[3,5,7,10]

explained by electrical leakage through the thin walls of the long narrow ductus reuniens.[6]

The major difference in technique between our present experiments and our previous measurements in saccule and utricle is the use of relatively large (30 to 40 μ) pipettes in the earlier experiments to allow the simultaneous collection of fluid for chemical analysis. In the present experiments we have used hyperfine electrodes such as were originally employed for the scala media. We thus avoided gross injury to the structures in the ampulla.

Our results are completely at variance with the measurements reported by Trincker.[14-17] The latter also form a self-consistent set with positive potentials of varying magnitude distributed throughout the membranous labyrinth. The potentials tend systematically to be greatest in the neighborhood of sensory cells, whether in the ampulla of the lateral or the superior canal or near the macula of the utricle.

For comparison with our own measurements, which are illustrated in Figures 3 and 4, we present a summary of Trincker's DC measurements. Some of them are taken from his original paper and others Dr. Trincker has kindly furnished us in correspondence. From his paper we translate:

"Relative to the perilymph the following resting potentials were measured inside the ampulla and the semicircular canal:

1. In the wall of the membranous labyrinth and ampulla —9.0 to —22.0 mv.
2. In the endolymph +38.5 to +43.0.
3. At the surface of the cupola ±63.0 to +75.5 mv.
4. In the interior of the cupola —6.5 to +75.0 mv.
5. In the crista ampullaris —38.5 to —57.0 mv."

The appearance of abrupt potential differences in the interior of the cupola Dr. Trincker attributes to the presence of hair-like processes of the sensory cells imbedded in the gelatinous material. In correspondence Dr. Trincker adds:

"Further along the curvature of the canal away from the ampulla, inside the crus commune of the two vertical canals, +9 to +14 mv.

Near the utricular end of the horizontal canal, +15 to +18 mv.

Inside the utriculus near the opening of the crus commune, +12 to +15 mv.

In recessus utriculi containing the sensory macula, the statolithic membrane and surrounding large jelly layer, +21 to +28 mv.

The jelly layer of the macula utriculi, +35 to +45 mv."

In the course of our correspondence with Dr. Trincker we have been unable to arrive at a satisfactory explanation for the difference in our two sets of experimental results, but there are certain minor differences in technique which must be considered in seeking an explanation. Trincker uses an operative approach from above and has studied chiefly the anterior and lateral ampullae. We employed a posterolateral approach and have studied the posterior and, less thoroughly, the lateral ampulla. Both of us have investigated the utricule and the saccule. In each laboratory the manipulation of the labyrinth has been reduced to a minimum and in each case hyperfine electrodes

that can penetrate the wall of the labyrinth without mechanical disturbance have been employed. We see no significant differences in our experimental manipulations.

A major difference, however, is the type of microelectrode. We have always used a micropipette filled with 3-molar KCl and a chlorided silver wire immersed in the solution within the pipette. Trincker employed electrodes of the type described by Svaetichin.[8] In this type the interior of a glass capillary is filled with silver solder. The tip is plated with rhodium and that in turn is covered with a deposit of platinum black. A platinum wire makes contact with the silver within the capillary. Trincker's "indifferent" ground electrode was an unchlorided silver wire inserted into one of the neck muscles.

It seemed to us that Svaetichin's metallic electrodes might be sensitive to differences in the chemical composition of perilymph, endolymph, intracellular material, or the gelatinous substance of cupola ampullaris or macula utriculi. Furthermore, because the electrical resistance of such an electrode is largely concentrated at the metallic surface and in the small layer of fluid immediately in contact with it, the measurements might be sensitive to differences in the specific resistance of the medium with which it is immediately in contact.

We raised these questions in correspondence with Dr. Trincker. He repeated his basic experiments, and in a letter dated 23 August 1958 he wrote,

> "I have repeated all important experiments, showing the methods to a foreign visitor. We found the measuring equipment previously described rather suitable for the use of high resistance microcapillaries and we got the same values of potential with fluid-filled electrodes as with the metal-filled ones. There was no doubt. I am sorry." *

A slight difference in the input circuits of our amplifiers and the differences in our ground electrodes may possibly still be of significance. In each amplifier circuit the microelectrode is attached to the grid of one input tube in a balanced differential amplifier. The two input tubes are in each case a carefully matched pair. Both are

* We particularly appreciate Dr. Trincker's courtesy and co-operation, not only in performing these additional experiments but in allowing us to quote fully from this and other correspondence. It is only fair to add that Dr. Trincker makes it clear that his major interest in his series of experiments has been in the changes of potential produced by movements in the endolymph and cupula rather than in the absolute values of the internal polarization, which has been our chief concern.

supplied from the same A and B batteries and thus make the output of the amplifier insensitive to fluctuations in battery voltage, etc. What is measured is the difference in the outputs of the two halves of a bridge circuit. The input grid of our control tube is grounded while Trincker connects his control tube to a second microelectrode similar to his exploring electrode. His reference electrode remains stationary in the perilymph and both his reference electrode and his exploring electrode measure a potential relative to the "indifferent" ground electrode in the muscle. This slight difference in circuitry may become important because Trincker's electrode system is not symmetrical. A silver wire is in contact with the tissues of the animal while the other contact is made through silver solder, coated with rhodium and in turn coated with platinum black. When fluid-filled electrodes were used, his metal-to-fluid contact was made with a bare platinum wire dipping into the potassium chloride solution. In both of Trincker's situations there was therefore an electrochemical potential difference between the two electrodes and the system was therefor probably more sensitive than ours to changes in the impedance of the electrodes and of the substances in which they are immersed. We are at a loss to suggest, however, how this greater susceptibility would give the systematic distributions of potential that Trincker describes.

Since the foregoing discussion was written we have had personal communications from three other investigators, in addition to Dr. Tasaki, who have independently made observations similar to ours.

Dr. César Fernandez writes that in the cat, recording from the ampulla of the lateral semicircular canal, the endolymph is at the same electrical potential as the perilymph, and also in the area of the cupula. In the sensory epithelium he finds a negative DC potential of about 30 mv. He uses glass pipettes of about 4 to 5 microns filled with Ringer's solution.

Dr. L. Gisselson told one of us (C.A.S.) that he had found that the DC potential is "low in the ampulla of the guinea pig."

Dr. G. A. Misrahy writes: "We placed a few KCl electrodes in the utricle, saccule and ampulla with results similar to yours. With metallic electrodes, all sorts of strange potentials appeared and we therefore abandoned . . . (them) feeling that the . . . potentials were an artifact due to contact potentials."

All of us including Trincker agree completely in regard to the intracellular negative potentials. The difference in results lies entirely

in the presence or absence of a positive polarization of the endolymph. In our search for an explanation we have even considered the possibility of a true biological difference between our guinea pigs and Trincker's "meerschweinchen," which he tells us are an inbred strain. This is a very remote possibility, but it cannot be completely dismissed.

SUMMARY

The electrical polarization inside the ampulla of the posterior and of the lateral semicircular canals of guinea pig have been measured, using microelectrodes less than 1 μ in diameter. Negative potentials, up to as much as —80 mv, were regularly encountered while the electrode tip was penetrating the wall of the membranous labyrinth and in the region of the crista. Most of these potentials were almost certainly intracellular in origin; others were found where the cupula should be. The potential of the endolymph between the wall and the crista was the same, within one or two millivolts, as that of the perilymph just outside the wall. Thus the electrical polarization of the endolymph of the semicircular canals is negligible, as it is in the utricle and saccule, and is not strongly positive, as it is in the cochlea.

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NOTE. In a letter received after this paper was in press Dr. Trincker reports the following measurements of potential differences between the endolymph in various parts of the vestibular system relative to the cochlear endolymph: utricle 38 to 69 mv; saccule 43 to 66 mv; curvature of canals 57 to 67 mv; ampullae 32 to 54 mv. The cochlear endolymph is positive relative to all the others. Dr. Trincker emphasizes the excellent agreement between these latest measurements and our conclusions. He states, "All potential differences recorded by one and the other group inside the endolymphatic system are of the same order of magnitude. The record of Figure 1, gained by Dr. Davis's group, could easily be likewise recorded by Dr. Trincker. All apparent differences must be only caused by the differently chosen reference points."

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LXXV

OBSERVATIONS ON THE MICROCIRCULATION OF THE COCHLEA

AN EXPERIMENTAL STUDY

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Some cases of sudden deafness and Ménière's disease are considered to be the result of disturbed circulation in the inner ear. However, it is difficult to detect the part and location of lesion in the organ by clinical examinations. Furthermore, as autopsies have been few, the cause and pathogenesis of these diseases are still matters of conjecture.

Studies of the blood vessels of the inner ear from functional and physiological aspects are essential. Recent in vivo observations of the inner ear vessels of animals have been designed to elucidate vascular accidents in the organ.[1-4] However, many problems are left unsolved because of difficulties in the techniques of micropreparation and photography.

It is my purpose in this presentation to report observation on cochlear blood flow and results of some drugs effects in order to obtain information on the characteristics of cochlear vessels.

EXPERIMENTAL METHOD

In the experiment, about 200 adult albino guinea pigs (both sexes) weighing 250 to 450 grams were used. They were anesthetized with intraperitoneal administration of 25% urethan (1 g/kg) and then tracheotomized.

The cochlea was approached ventrally through the bulla tympanica. With the aid of the Zeiss-Otoskop, the apical or the third coil of the cochlea was fenestrated with a fine probe after partial

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removal of the mucous membrane which covered the cochlear bony capsule.

Using the microscope especially designed for the purpose (40 to 240 x), small vessels of the spiral ligament and stria vascularis could be observed through the fenestra. The field observed was not heated, but sometimes a heat absorbing filter was used to avoid excess heat of illumination.

After heparinization (3 mg/kg), a glass canula with a fine polyethylene tube at the top was inserted centripetally to the contralateral carotid artery in order to measure blood pressure directly. The glass canula was connected with a mercury-manometer. Great care was taken in the procedure to avoid injury to the vagus nerve. Simultaneous recording of the breathing was made on smoked paper by connecting with the tracheal tambour.

After an in vivo observation was finished, the spiral ligament together with the stria vascularis was removed to examine details of the vascular pattern and vascular structure in these tissues.

RESULTS

The vessels observed in the field of the spiral ligament and stria vascularis were divided into five groups.

1. *The Radiating Arteriole.* The arterial vessel ran over the scala vestibuli part of the spiral ligament basalwards. Observation through the large fenestra showed segmental and parallel distributions of the vessels short distances apart. Flow time of plasma space or Plasmalücke and white corpuscles required in passing a given distance of the vessel indicated rate of blood flow. In the radiating arteriole, order of flow rate is about 500 μ/sec or more. This was the same as the value that was measured through the thin bony capsule of the cochlea before fenestration began. Measurement of flow time of the plasma space was particularly difficult in cases of high velocity. Oscillation of the vessels seemed to be recognized in these cases.

Adventitial cells were recognized here and there. Change in diameter of the vessels was not observed. At a right angle to the arteriole, small vessels ran parallel to and above the attachment part of Reissner's membrane which was sometimes observed.

2. *The Strial Capillary.* The blood flow in the stria vascularis was at a right angle to that of other vessels in the spiral ligament. The

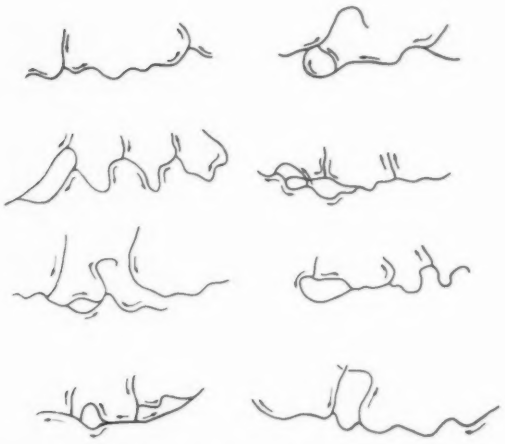

Fig. 1.—Schematic drawings of vascular patterns and directions of blood flow in the limbus.

flow was slower than in the arteriole, venule or arteriovenous anastomoses. The diameters of the strial capillaries were usually larger than those of other vessels. However, they were variable among the strial capillaries in the same field. As these capillaries were located under the thicker part of the spiral ligament, the blood flow within them was observed somewhat indistinctly.

Oscillation and vasomotion were not observed in the stria. There was no closed capillary. Direction of blood flow was reversible according to local pressure change, although under normal conditions the direction did not change.

The blood flow in the stria vascularis is apparently different from others and gives one an impression that it plays a significant role in the cochlear metabolism.

3. *Arteriovenous Anastomosis.* The vessel coursed from the radiating arteriole directly to the venule in the thicker part of the spiral ligament. Occasionally bead-like flow of the blood corpuscles, "beads stream" was observed in the vessel. The occurrence was independent of the other arteriovenous anastomoses. The phenomenon was probably ascribed to action of the sphincter at the orifice of the vessel. Generally speaking, the blood flow in the arteriovenous anastomosis was comparatively variable in contrast to the other flows.

4. *The Venule.* The venule was located in the lower spiral ligament. Blood from the radiating arteriole, strial capillary and arteriovenous anastomoses drained into it. Because of anatomical restriction, the venules in the apical coil were not observed clearly even though a large fenestra extending to the third coil was opened. They appeared to course basalwards after a short distance and disappeared in the depth.

5. *The Blood Vessel Under the Spiral Prominence.* Blood flow existed below the stria vascularis, though it was not always observed. There was no anastomosing vessel among them. Derived from the arteriole, it coursed behind the stria vascularis and below it in a spiral direction.

Sometimes, it seemed to me that the vessel was a modified preferential channel. Many branches left the vessel going to the venules of the lower spiral ligament.

BLOOD FLOW IN THE LIMBUS SPIRALIS

Another system of blood supply was observed through the spiral ligament in the deep part of the cochlea, though it was not always possible to observe it (Fig. 1). The vascular pattern was simple in contrast to that of the spiral ligament and the stria vascularis.

Blood flow originated suddenly from the modiolus. It flowed in a spiral direction for a short distance near the margin of the limbus spiralis after it flowed centrifugally from the modiolus, then it returned to the modiolus and disappeared. The flow rate of the blood was more rapid than in the spiral ligament and stria vascularis. With a fall of blood pressure due to administration of tetraethylammonium bromide, blood pathways disappeared partially in some areas and in others the flow rate became slow. But the picture returned to normal following adrenalin injection (Fig. 2).

EFFECTS OF DRUGS UPON THE INNER EAR VESSELS

Adrenalin. No visible changes in blood vessels were observed with dilute solution of adrenalin which markedly contracted mesenteric vessels. However, administration of large doses (0.05 to 0.25 mg/kg) resulted in change of blood flow. Approximately 20 seconds after the intramuscular injection, slight enlargement of vessel calibers was observed in all vessels. "Beads stream," if present, changed to vigorous and continuous blood flow. Sudden increase in flow rate of

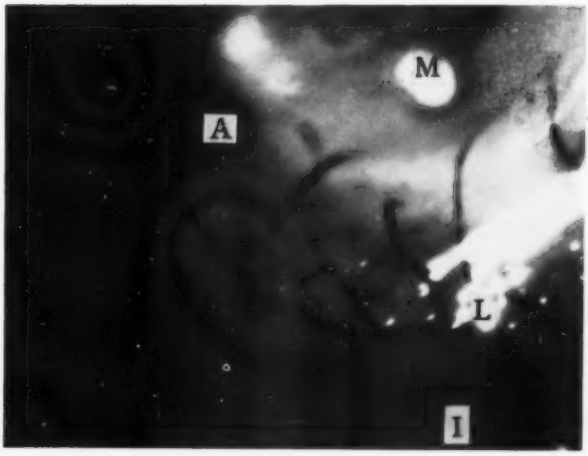

Fig. 2.—Vascular patterns observed in the limbus. India ink injected. 60 x). Blood stream (A) disappeared with a fall of blood pressure due to injection of tetraethylammonium bromide. *L.* Spiral border of the limbus. *I.* Spiral borders below the inner pillar and the tunnel. M. Modiolus.

the blood occurred in all vessels. Systemic blood pressure was elevated rapidly and breathing was restricted simultaneously. After a short period of time flow rate of the blood in these vessels began to decrease and returned earlier to previous circumstances than did the blood pressure. This is discussed later.

In one case, capillarization was observed in the stria vascularis. A part of the strial capillary was filled with plasma without flow. After adrenalin injection the stream began to flow.

Nor-adrenalin. Doses used in the experiment ranged 0.1 to 1.0 mg/kg. With blood pressure elevation, the flow rate in the radiating arteriole increased. Changes in flow in the stria vascularis are not so remarkable as those of the radiating arteriole provided the pressure elevation was about 40 per cent. Furthermore, if changes occur, the blood flow observed in the stria vascularis seemed to return earlier to the previous condition than it did in other vessels.

Pilocarpine. After intramuscular injection (0.1 to 0.4 mg/kg), the plasma spaces observed in the radiating arteriole increased in num-

ber. Sometimes enlargement of these spaces was also observed in the vessel. The flow rate decreased slightly in the radiating arteriole and other vessels. But visible changes in vessel diameter were never observed. In the strial capillary, these changes were not evident as compared with those of the radiating arterioles and other vessels of the spiral ligament.

Marked lacrimation and salivation also occurred.

Atropine. Administration of atropine (0.1 to 0.3 mg/kg) produced no visible change in the rate of blood flow, diameter of vessels or in the blood stream.

However, atropine could block the influence of pilocarpine upon the blood stream particularly observed in the radiating arteriole. Atropine also caused the fall of blood pressure due to pilocarpine injection to return to the former level.

Acetylcholine. Administration of acetylcholine (8 to 50 mg/kg) decreased flow rate in the radiating arteriole and strial capillary. However, no apparent change was observed in number and length of the plasma space in the vessels. In the strial capillary flow rate decreased slightly.

Active vasodilation was not observed in any other vessels.

Histamine. Administration of histamine (0.2 to 0.3 mg/kg) reduced numbers of the plasma spaces. No remarkable change was observed in the strial circulation. In cases of large doses (1.5 mg/kg), blood flow in the radiating arteriole became sluggish and in arteriovenous anastomosis decreased before strial flow became so.

COMMENT

The experiment showed extreme stability of the cochlear small vessels.† The cochlea afford us a new field for study of the microcirculation in relation to brain blood vessels because it tolerates long time observation and has a simple vascular pattern which derives from *A. labyrinthi.*

Perlman and Kimura[2] have already discussed the refractoriness of the cochlear small vessels to several kinds of stimuli. They observed small vessels of the spiral ligament and stria vascularis unchanged by blockade or stimulus of the cervical sympathetic nerve

and other stimuli which might influence vessels of other parts of the body. From another study of Perlman, Kimura and Butler[5] on the cochlear circulation during hypothermia, none of vessels in the fenestra showed definite changes in diameter even in extreme cooling which brought about arrest of the heart and blood flow.

It is possible that surgical procedure per se may give rise to changes in blood flow, and that we may have always observed an altered blood flow. However, a consideration of the vascular structure of these small vessels is necessary to understand this refractoriness.

A true capillary is the endothelial tube without any contractile element and it exhibits neither contraction nor dilation. Accordingly change in diameter of a capillary, if observed, may be passive following a change in the blood stream of proximal arteriolar vessels.

However, narrowing of the capillary lumen may occur without contraction. Sanders, Eberth and Florly[6] observed occlusion of the lumen due to swelling of the endothelial cell without change in outside diameter using the rabbit's ear chamber method. Linzbach[7] observed in the endothelial cell of the human aorta swelling of the "hyaloplastische Deckplatte." This phenomenon is different from constriction of the capillary.

The strial capillary and vessels near the part of Reissner's membrane are true capillaries. Accordingly, it is not surprising that these vessels seemed to be invariable.

Krogh[8] observed that closed capillaries in the muscle became open when it worked. According to Petrén,[9] capillarization was observed histologically in motor area of the guinea pig's brain after muscle work of several weeks. However, in the cochlea, closed capillary is not evident. Circulation in the cochlea may be almost constant at any time.

The radiating arteriole, less than 20 μ in diameter, is preferably called the metarteriole or the precapillary, because the word arteriole gives one an impression that it possesses a thick muscle coat in its wall and a diameter of 20 to 50 μ. As to plasma space frequently observed in the blood stream of the radiating arteriole, little is known. It probably indicates frequent occurring of temporary contraction and relaxation of proximal arterial vessels. Its appearance at comparatively the same interval may be a sign of the vasomotion. The frequency ranged from 40 to 60 a minute.

Arteriovenous anastomoses are distributed all over the body.[10] From Staubesand's observation,[11] there are several types of arteriovenous anastomoses according to the size of the artery and vein. The simplest is a channel which bridges from an arteriole to its corresponding venule. The vessels observed in the spiral ligament appear to be of this type. The most complicated consists of glomus cells around the anastomosing vessel.

As to significance of arteriovenous anastomoses in the cochlea, Agazzi[12] considered that they serve to regulate the strial circulation. From his supposition, it may act as a bypass when blood flow in the stria vascularis, which regulates secretion of the endolymph, is excessive in quantity. Weille[13] considered it as functioning to regulate temperature in the middle and inner ear.

Krogh[8] considered that the main function of the vessel is to supply enough blood to projecting parts of warm-blooded animals to keep them warm when exposed to low temperature. When we think of the existence of the vessel only in warm-blooded animals and of the ease of conduction of surrounding temperature to the inner ear, it may be that temperature regulation is one of the important functions of the vessel.

There are two kinds of blood circulation in the organ. One is the blood flow that is necessary to maintain tissue metabolism during rest. The blood flowed through a preferential channel. The other is the flow through arteriovenous anastomoses in which a considerable amount of blood flowed even in rest. But when the organ began to work, the vessel closed at once and blood flowed into the preferential channel.[14]

Arteriovenous anastomosis in the inner ear observed in the experiment is somewhat different from the above mentioned conception. When decrease of blood flow to the inner ear occurred following a fall of blood pressure, the flow in the vessel may decrease before strial blood flow begins to decrease as if it preserves strial circulation.

When increase of blood pressure occur, the reverse occurs. The function of the arteriovenous anastomoses in the spiral ligament is to preserve constant blood flow of the stria vascularis especially when blood flow to the inner ear is altered. In relation to activity of the vessel, the role of the sphincter must be considered. It is accepted that the strial vessel has intimate relation to the inner ear metabolism. However, regulation of the strial circulation may be in large part dependent on the arteriovenous anastomoses.

It is not certain whether or not a critical closing pressure[15] exists, and, if so, whether it is relevant to the activity of the sphincter.

Attention must be given to the venule-vein system. According to Lutz and Fulton,[16] 60 to 75% of peripheral circulating blood is in venous system at any time. Bleeding, thrombosis and petechial formation are apt to develop in the area. In the inner ear, the venules are permeable to dye-stuffs.[17] Furthermore, the internal surface of the venule is at least twice as large as that of the arterial vessels in the upper spiral ligament. The venule-vein system is not only a container for the venous blood, that is, a capacity vessel, but it may be endowed with special functions.

Irregularly looped blood vessels observed in the limbus are derived from the secondary branches of the A. cochleae propria. Shambaugh[18] and Smith[19] called these vessels borders of capillary areas and spiral border of the limbus respectively. Rapid blood flow in the vessels is impressive in contrast to slow strial flow. Furthermore, partial blood flow and a decrease of flow rate of the remainder with fall of blood pressure before the flow in the spiral ligament stops indicate that the vessels are not so important as the stria vascularis for the metabolism of the inner ear and serve as a reservoir of blood to the stria vascularis and spiral ligament.

The local application of drugs of vasodilation and vasoconstriction gave rise to no visible change. Such changes as are observed may be chiefly due to the effects of drugs on the systemic circulation. Changes in the inner ear vessels may be hidden behind the systemic changes of circulation. Effects of drugs on the inner ear vessels are difficult to evaluate.

Mygind[20] demonstrated histologically that dilation of the strial capillary occurred after injection of adrenalin in the guinea pig (paradoxe Reaktion). He also observed construction of the vessel by histamine injection. These are probably due to secondary changes of systemic blood pressure as he supposed. With blood pressure elevated, the strial capillary became somewhat large in diameter, and the blood flow rate in it increased.

Histological examination at this time probably showed an enlarged strial capillary. This is a passive change and not a dilation of the vessel. The narrow strial capillary after histamine injection may be due to a decrease of blood flow to the inner ear following fall of blood pressure.

According to Schicker's experiment[21] in the guinea pig, no significant changes of the inner ear vessels were observed after adrenalin (5 mg s.c.) or histamine (5 mg s.c.) injection.

Seymour and Tappin[22] also observed the effect of adrenalin upon the arteriole and strial capillary. They noted that vessels constricted, though it was not as well marked as in the vessels of the extracranium.

The strial capillary does not possess any contractile element in its wall. Therefore, constriction of the vessel seemed to be unlikely, except for that obliteration due to the swelling of endothelial cell of the strial capillary produced by adrenalin. Adrenalin may act on the wall of the radiating arteriole, as arterial side of vessel is more highly reactive to most constriction influences (Zweifach[23]). However, it does not constrict mainly because of the sparsely distributed muscle cells of the vessel wall observed here.

Difference of effects of adrenalin and nor-adrenalin upon the inner ear vessels considered here was not so distinct. However, strial circulation seemed to be much influenced by adrenalin, though in cases in which extreme hypertension was brought about the same result was obtained by both drugs. According to King,[24] increase of oxygen consumption of the brain after adrenalin injection indicated that the drug was relevant to metabolism of the brain, whereas it was not significantly altered by nor-adrenalin. Difference of the effects in the inner ear circulation might be dependent upon the circumstance whether or not the inner ear metabolism is influenced.

As to action of histamine on the brain vessel, many investigators have reported dilation and increase of cerebral blood flow. With nitrous-oxide technique of Kety and Schmidt, Alman[25] investigated influence of histamine on the circulation of human brain. Intravenous injection of histamine was designed to maintain the mean arterial pressure at 5 to 50 mm Hg below that of the immediately preceding control period. This resulted in a moderate reduction of resistance of cerebral blood vessel indicating vasodilation of the cerebral vessels. Cerebral blood flow and oxygen utilization were not significantly influenced. Messen[26] observed ischemic condition of the retinal circulation of the dog during collapse due to intravenous injection of histamine.

In the inner ear, decrease in the number of plasma spaces observed in the radiating arteriole are probably indicative of dilation of the proximal vessel. However, blood flow to the inner ear may not be

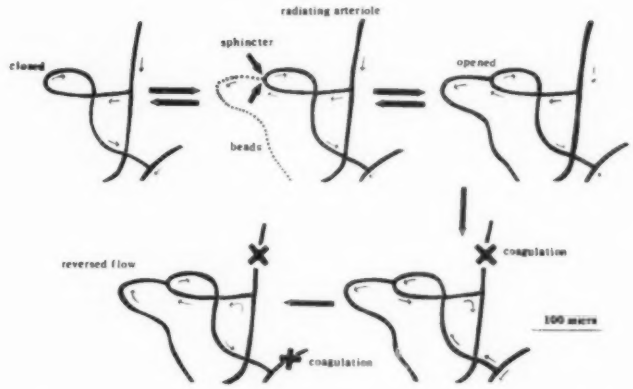

Fig. 3.—Changes in direction of blood flow. Three figures above indicate spontaneous change and two below after coagulation of the blood due to trauma.

influenced by dilation, because concomitant fall of blood pressure may occur.

Increase of the plasma spaces in number and length after pilocarpine injection may be indicative of contraction of the proximal vessel. These changes were easily antagonized by atropin injection. This is reasonable because pilocarpine possesses muscarinic effects of acetylcholine which is blocked by atropine. However, it is uncertain why muscarinic action influences the appearance of plasma spaces in the radiating arteriole.

Finally, the actions of drugs used here on the small vessels of the stria vascularis and spiral ligament were not clearly observed, though some changes of the proximal arterial or arteriolar vessels could be inferred. Changes in the blood stream of the inner ear were mainly secondary to an altered systemic circulation.

BLEEDING OF THE INNER EAR VESSELS

Injury to the radiating arteriole of the apical or third coil resulted in a brisk and pulsative bleeding into the cochlea. However, this is interrupted after several minutes, resulting in most cases in a change in the direction of blood flow in periphery vessels (Fig. 3). Sometimes the blood flow was stopped in the stria vascularis immediately

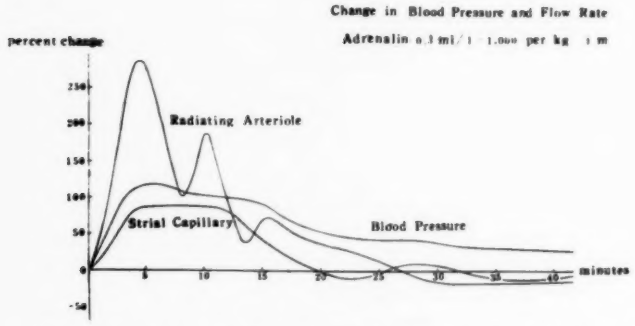

Fig. 4.—A relation of flow rate and blood pressure. Adrenalin injection.

after bleeding of the supplying radiating arteriole. Therefore, segmental disturbance of strial capillary had occurred. Thrombi were observed in both ends of the vessels without marked constriction. Occasionally, temporary bleeding was observed after hemostasis due to elevation of the blood pressure.

Bleeding in the region of the inner ear may easily cease provided the mechanism of blood coagulation is not disturbed. This is based on the finding obtained in the apical or third coil. It is probably not the same in other coils, as the blood pressure of the radiating arteriole is probably higher basalwards.

Elevation of the blood pressure to three times the previous level did not result in hemorrhagia per rhexin in the intact spiral ligament and stria vascularis throughout the cochlea, although it was uncertain whether hemorrhagia per diapedisin occurred.

RELATION BETWEEN SYSTEMIC BLOOD PRESSURE AND BLOOD FLOW IN THE INNER EAR

Influence of changes in the systemic blood pressure upon the inner ear circulation is of utmost importance. Does there exist regional regulation of the cochlear circulation? Does the circulation exhibit parallel pressure changes in all parts of the cochlea?

Flow rates were measured following elevation or fall of blood pressure at the radiating arteriole, strial capillary and sometimes

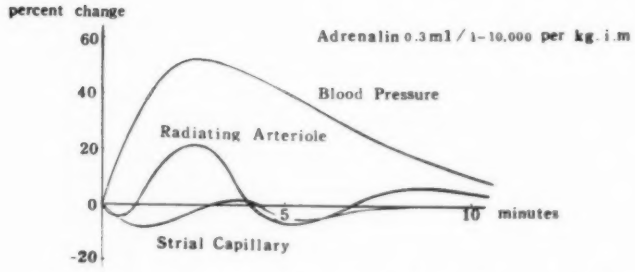

Fig. 5.—A relation of flow rate and blood pressure. Adrenalin injection.

arteriovenous anastomosis at intervals of a few minutes. However, "bead streams" frequently observed in the arteriovenous anastomosis usually made it difficult to measure flow rate of the blood. Pressure changes were induced with intramuscular administration of adrenalin or Pendiomide.® Figures indicate the per cent change of systemic blood pressure and flow rate (Figs. 4, 5, 6).

Adrenalin: Administrations of the same doses were not always able to produce the same changes in the pressure chiefly because of individual difference of susceptibility and depth of anesthesia. Elevation of blood pressure to 50% brought about little change in flow rate of the strial capillary, in spite of marked change in blood flow of the radiating arteriole. The circulation may be regulated peripherally. However, above the 50% level, the higher the blood pressure is elevated, the greater flow rate of blood in these vessels. Both duration and magnitude of changes in the strial capillary were not so remarkable as those in the radiating arteriole. Circulation of the strial capillary tended to come back earlier to the previous state.

Pendiomide (N, N, N^1, N^1 -3-pentamethyl-N, N^1-diethyl-3-aza-pentylene-1.5-diammonium-dibromide CIBA): Fall of the blood pressure down to 20% brought about no distinct change in blood flow of the small vessels of stria vascularis. However, below the level, strial circulation was not compensated.

It is difficult to measure change in blood volume of each part of the inner ear at a given time. No visible change in diameter of vessels considered here were obtained, although vasomotion due to the sphincter existed. This leads to the conclusion that changes in flow rate may

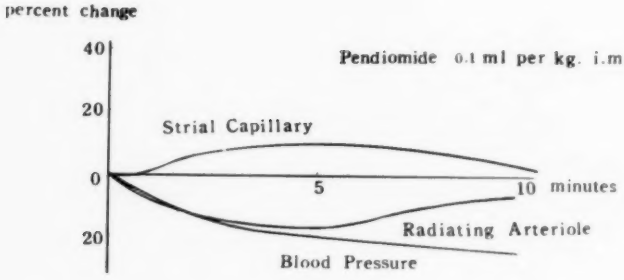

Fig. 6.—A relation of flow rate and fall of blood pressure. Pendiomide injection.

indicate approximately those changes in blood volume in these vessels. A mesh-like vascular pattern of the stria vascularis gives one an impression that it is not significant to refer to the circulation from rate data of a given capillary. The width of the stria vascularis becomes narrower towards the apical coil without a change of interstice of the mesh. Therefore, the vascular pattern of the apical coil in the field is comparatively simple. Any procedure producing changes produced similar changes in blood flow throughout the strial capillary. Conjectures are made from these observations.

Change in systemic blood pressure within certain range gave no apparent change in the circulation of the strial capillary. The manner of regulation in the stria vascularis is of paramount importance. This peripheral vascular homeostasis may be due to a structural organization of the strial capillary, abundance of arteriovenous anastomoses and vasomotion of the sphincter. Change in flow rate of the radiating arteriole subsided before blood pressure returned. It is, however, uncertain whether or not there exists regulatory mechanism in the cochlear artery.

SPHINCTER OBSERVED IN THE SPIRAL LIGAMENT

Running over the scala vestibuli, the radiating arteriole divides itself into several branches in the upper spiral ligament. It has been occasionally observed that continuous blood stream becomes "beads" like stream after passing through a region where metarteriole divides. Red corpuscles flowed with a constant interval in the channel, though

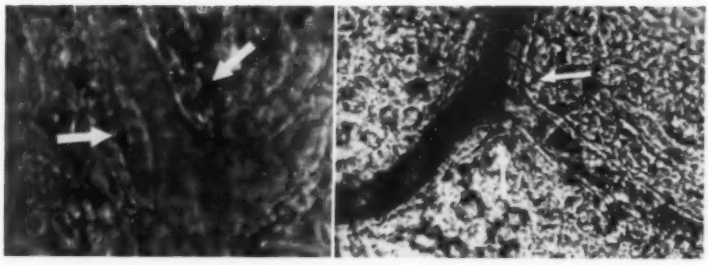

Fig. 7.—Sphincter. Beads stream appeared after passing through the region of the vessel. Arrows indicate sphincters. (400 x and 200 x resp.)

the interval is variable at different times even in the same vessel. This phenomenon was observed in certain vessels and not in others.

This is probably due to a periodic opening and closing of the vessel wall that is independent of the neighboring vessels. However, sudden stop and start type of the blood flow was not observed in the spiral ligament. Frequency of these periodic movement was variable. In some cases, it is too frequent to measure it by visual criteria.

The phenomenon was observed in the arteriovenous anastomoses. Vasomotion of the sphincter probably regulates circulation of the stria vascularis and spiral ligament. As is shown in Figure 3, the sphincter permitted reversals of blood flow. The direction of blood flow in the capillary network changes in consequence of local blood pressure changes. A sphincter per se was not detected clearly during the in vivo observation. Careful examination of the part after removal of the spiral ligament, however, revealed the cell around the orifice of the vessel (Figs. 7, 8).

It is an important problem whether or not the sphincter was supplied with nerve fiber. It was not observed in the experiment.

Lorente de Nó[27] found vasomotor nerve fiber in the modiolus, but not in other parts of the labyrinth. According to Smith's observation,[19] unmyelinated nerve fibers were traced up to the wall of the coiled secondary branches of the cochlear artery. In the wall of the radiating arteriole and strial capillary no fibers were observed. This is the same with the result obtained by Perlman and Kimura. However, von Euler[28] demonstrated that nerve free vascular smooth muscle

from human placenta reacted to both epinephrine and acetylcholine. Accordingly it is not surprising that the cell may display a myogenic activity without a nerve supply.

Chambers and Zweifach[29] observed precapillary sphincter in mesenteric capillary of the frog. Nicoll and Webb[30] found a similar structure called "Indian Club" in the bat's wing. Fulton and Lutz[31] demonstrated that the sphincter may act independently of the nearby connecting arteriole in the retrolingual membrane of the frog.

In the spiral ligament of the inner ear of the guinea pig, a sphincter could not be identified by Perlman and Kimura.[32] Schicker,[21] however, found nuclei of the pericytes in the vessels where the capillary coursed forward. This led him to suspect that they may be contractile, although pericytes are generally considered not contractile.

The cells observed in the present experiment are probably relevant to vasomotion by myogenic automaticity.

Further investigations are necessary to determine whether or not stimuli or change of environment call forth myogenic activity. It is peculiar in the spiral ligament that the sphincters were located at orifices of the arteriovenous anastomoses. The regulation of the blood supply to the stria vascularis may be dependent upon the activity of the sphincters. Dysfunction of the sphincters may lead to a disturbance in the inner ear circulation.

SUMMARY

1. The small vessels of the stria vascularis and spiral ligament were observed in the cochlea of living guinea pigs. Blood streams in these vessels showed extreme stability and were durable throughout a long observation period.

2. The actions of several drugs on the vessels were negative, chiefly because of scarcity of contractile elements in the vascular wall. However, certain changes due to altered systemic circulation and responses of proximal vessels were recognized in these vessels.

3. Several types of vascular patterns in the limbus were reported. The blood flow showed rapid and segmental distribution. The significance of the blood flow was discussed.

4. Vascular homeostasis probably existed in the microcirculation of the stria vascularis. In the process, action of the sphincter which is located at the orifice of the arteriovenous anastomosis might play an important role.

5. Characteristics of the stria circulation are discussed.

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LXXVI

STUDIES OF FACTORS CONSIDERED RESPONSIBLE FOR DISEASES OF THE EXTERNAL AUDITORY CANAL

III. A COMPARISON OF LIPIDS IN NORMAL AND INFECTION-SUSCEPTIBLE EARS

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It has been postulated that the absence of the normal protective lipids which coat the skin of the external ear canal may be a major factor contributing to the pathogenesis of certain types of external otitis.[1] The oily covering may act as a mechanical or chemical barrier and prevent micro-organisms from penetrating the top layers of the skin. There have been reports of an absence of cerumen in patients with external otitis, but it is not clear whether such a deficiency is a cause or one of the effects of the disease.

The purpose of this study was to answer two questions. Is there a difference between the amounts of lipids which may be obtained from the skin of the ear canals of patients susceptible to acute diffuse external otitis and those with no history of external ear disease? Does the lipid material on the skin of the normal external ear canal possess any particular antibacterial properties which are not present in the lipids obtained from infection-susceptible ears?

The self-sterilizing ability of the skin and its secretions has been shown by many investigators. Rebell *et al.*[2] found that gram-negative bacilli survived for much longer periods of time on skin washed with organic solvent than on skin with an undisturbed lipid cover. Burtenshaw[3] prepared ether and alcohol extracts of the skin, hair, cerumen and nails and tested them against a number of common bacteria. The extracts had a strongly bactericidal effect on *Streptococ-*

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cus pyogenes, Streptococcus viridans and *Corynebacteria diphtheriae*, but none on *Bacterium coli* and *Bacterium typhosum*. Some strains of *Staphylococcus aureus* and *Staphylococcus epidermidis, albus* were partly inhibited.*

Schäfer and Schönfeld[4] used various methods to test the bactericidal action of ether-alcohol extracts of normal ceruman. Their results showed that *Beta-hemolytic Streptococcus* was most often inhibited, whereas *Non-hemolytic Streptococci* were seldom affected and *Staphylococcus aureus* was not inhibited. Both *Pseudomonas aeruginosa* and *Aerobacter aerogenes* were not inhibited, while some strains of *Escherichia coli* and Proteus were.

Perry and Nichols[5] found that cerumen had no effect on *Micrococcus albus* and *aureus, Corynebacteria, Streptococcus pyogenes, Bacterium subtilis, Escherichia coli* and *Pseudomonas aeruginosa.*

The microbiological flora of the diseased human external ear canal has been studied extensively. Senturia[6] and Singer *et al.*[7] reported that a high percentage of cases of diffuse external otitis showed a gram-negative bacillus, predominantly the *Pseudomonas aeruginosa.*

Senturia and Liebmann[8] experimentally produced disease in the external ear of the cat by infection with *Pseudomonas aeruginosa.* They found that infection occurred more readily if instillation of the organism was accompanied by trauma or lipid removal from the ear canal. However, Senturia and Carr[9] later showed that removal of the surface lipids did not appear to increase the survival time of *Pseudomonas aeruginosa* instilled into the cat ear canal even when a very dilute suspension of the organism was used.

METHODS AND TECHNIQUES

Two groups of subjects, normal and susceptible, were chosen for a quantitative comparison of the amounts of lipid which were obtained from their external ear canals. The specimens were either "casual"† or collected at a specified interval after thorough cleansing of the canals. The normal group consisted of five persons (10 ears) with no histories of external ear disease. The susceptible group was made up of eight patients (14 ears) who had previously been treated for diffuse external otitis two or more times, and who were presently

* Bacteriological terminology throughout is that of the author being quoted.

† "Casual" specimens are those obtained from the surface of the ear canal at the beginning of the period of observation, without previous cleansing or treatment of the canal.

in a quiescent period. Only one subject had an uncomplicated history of diffuse external otitis, whereas the others had had occasional bouts of neurogenic external otitis or otomycosis alternating with the diffuse infections.

Bacterial cultures of the ears were made routinely prior to the taking of lipid specimens, and the swabs were inoculated onto blood agar and MacConkey plates. Biochemical reactions for identification of the gram-negative bacilli were performed according to procedures suggested by Edwards and Ewing.[10] The coagulase test was performed on all Staphylococci, regardless of hemolytic activity or pigmentation of colonies.

MEASUREMENT OF ETHER-SOLUBLE SUBSTANCES

All specimens were obtained by wiping the ear canals with ether-moistened cotton swabs in a standardized manner previously described.[11] Casual specimens were taken and the ear canals were irrigated with warm 3 per cent saline solution, then gently dried with cotton swabs. Immediately thereafter specimens were taken to check on the thoroughness of the cleansing procedures. Subjects were asked to refrain from cleaning or rubbing their ears, and one week later cultures and specimens were again taken in the prescribed manner.

The organic matter in the cerumen which was extracted from the swabs with redistilled ethyl ether in a mocro-Soxhlet apparatus constituted the "ether-soluble substances" (ESS). The ESS, which are primarily lipid, were determined quantitatively by a colorimetric method.[12]

BACTERIAL EFFECTS OF ESS

Two methods were used for an *in vitro* evaluation of the relative bactericidal effects of ESS from the ears of two normal and two susceptible subjects. Because *Pseudomonas aeruginosa* is very frequently cultured from ears with diffuse external otitis, it was used as the test organism. The strain used was obtained from a patient with acute diffuse external otitis. Since the growth of *Beta-hemolytic Streptococcus* has been shown previously to be inhibited by extracts of cerumen,[3,13] the same tests were made with this organism, obtained from a patient with otitis media, as a form of control.

The ether extracts of the several specimens from one person were combined to make each test extract. The ether was removed

TABLE I

ETHER-SOLUBLE SUBSTANCES IN CERUMEN FROM NORMAL AND SUSCEPTIBLE SUBJECTS

	CASUAL (MG.)	7-DAY (MG.)
Normal Subjects:		
Mean (10 specimens)	3.56	1.08
Standard Deviation	4.87	1.03
Standard Error	1.54	0.33
Range	0.21-16.5	0.32-3.61
Susceptible Subjects:		
Mean (14 specimens)	2.91	1.18
Standard Deviation	4.28	0.82
Standard Error	1.14	0.22
Range	0.03-13.5	0.14-2.71

by evaporation before the ESS were brought into contact with the culture medium and the test organisms.

1. *Disc Method.* Filter paper discs were impregnated with amounts of ESS ranging from 0.2 to 1.2 mg and were placed on veal-infusion agar plates, inoculated with the test organism.

2. *Tube Method.* Similar amounts of the same ESS specimens were placed in sterile 3 ml test tubes and mixed with 0.5 ml of Trypticase soy broth containing the test organisms. Where necessary each of the tubes was then subcultured onto blood agar to determine the presence or absence of growth.

RESULTS

The usual bacterial flora was found in the ear canals of the normal subjects and in all but one of the susceptibles. A *Proteus vulgaris* was cultured from this susceptible ear on the day of cleansing and again on the seventh day. None of the Staphylococci cultured from either the susceptible or the normal ears were coagulase-positive.

A summary of the statistical analysis of the data from the ESS determinations is shown in Table I. Mean casual ESS was 3.56 mg

± 4.87 (Standard Deviation) for normal ears, and 2.91 mg ± 4.28 for susceptible ears. Data from both ears of each person were handled individually. Seven day averages for normal and susceptible ears were 1.08 ± 1.03 and 1.18 mg ± 0.82 respectively. Individual variations were great in both groups. There was no significant difference between the means of the normal and susceptible ears ($P > 0.7$).

In the tests for bactericidal effects of ESS upon *Pseudomonas aeruginosa* there was no inhibition of the growth of the organism regardless of the amount of ESS used. All the plates containing the discs were completely overgrown with Pseudomonas. Profuse growth with a heavy pellicle was observed in all the tubes.

In contrast, the bactericidal effect of ESS upon the *Beta-hemolytic Streptococcus* was striking. With the disc method, zones of inhibition ranging from 10 to 12 cm in diameter were present around all the discs except the control. The zones of inhibition were as great for the discs containing the least amounts of ESS as were evident for those containing higher amounts. In the tube method, no growth occurred in the subcultures except from the control tubes.

COMMENT

It is interesting to note that the bacterial flora of the normal and susceptible ear canals were essentially similar to the normal flora which has been described previously.[6] The only exception was a strain of *Proteus vulgaris* in one susceptible ear which persisted despite the irrigation and cleansing procedures. The reason for this persistence and the general susceptibility of some ear canals to infection by enteric gram-negative bacilli is still not known. Actually, a higher incidence of gram-negative bacilli, particularly *Pseudomonas aeruginosa,* had been anticipated among the susceptible group in view of the recognized difficulty in eradicating these organisms from infected ear canals.

The infection potential of coagulase-positive Staphylococci in various areas has been the cause of much concern. Studies in progress show that these organisms are sometimes found in the diseased ear canal. Their absence, however, from the ears of our susceptible subjects in the quiescent state suggests that when such organisms are found they are exogenous to the ear canal.

Mean values for seven-day specimens of ESS reveal that the susceptible ears recovered their lipid coating as rapidly as did the nor-

mal ears. This fact, together with the lack of a significant difference between the means for casual specimens of the two groups, strongly indicates that the sebaceous glands in these susceptible ears were not destroyed by the disease process. It would not, however, eliminate the possible development of a malfunction of the apocrine glands in the ear canal similar to that shown by Senturia and his associates.[14]

It is likely that the fatty acid portion of the lipid matter is mainly responsible for the bactericidal effects of cerumen extracts. Fatty acids as a whole are generally more effective bactericidally against Streptococci than against gram-negative bacilli, including *Pseudomonas aeruginosa*. On the basis of previous work by his group, Wheatley[15] reported that human skin surface lipids, composed of both sebum and epidermal lipids contain about 28 per cent free fatty acids (C_7-C_{18}), 42 per cent combined fatty acids, and 30 per cent unsaponifiable matter. Haahti *et al.*[16] found that the fatty acid composition of normal cerumen is very similar to that of the skin surface lipids of the same individual.

Our own results in which *Beta-hemolytic Streptococci* were inhibited by ESS from cerumen, while the *Pseudomonas aeruginosa* were not, are thus in agreement with the usual findings regarding the action of fatty acids.[3,13] This *in vitro* activity of cerumen ESS is also in accord with the fact that *Beta-hemolytic Streptococci* are rarely found, while Pseudomonas are frequently cultured from the external auditory canal of diseased ears.

SUMMARY

Cerumen specimens were taken from the auditory canals of persons who had no histories of external ear disease and also from patients who were known to be susceptible to acute diffuse external otitis. The ether-soluble substances in these secretions from the two groups were compared with respect to the amounts accumulated in a given period and with respect to their bactericidal properties against two organisms: *Beta-hemolytic Streptococci* and *Pseudomonas aeruginosa*. It was found that there were no significant differences between the measured amounts or bactericidal properties of the ESS from the control and susceptible groups.

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LXXVII

STAPES SURGERY: SELECTION OF THE PATIENT

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During the seven years since re-introduction of the stapes operation by Rosen,[1] great improvements have been made in surgical technique. One of the most important of these improvements was the concept of total stapedectomy with vein graft and polyethylene prosthesis[2] and later the use of a wire prosthesis.[3] These techniques have led to improved results (Fig. 1). Eighty per cent or more of the patients undergoing stapes surgery at the present time can expect permanent improvement in hearing to within 10 decibels of the preoperative bone conduction level.

As techniques and results improve, the indications for surgery broaden. The purpose of this paper is to discuss the selection of the patient for stapes surgery in view of these improved surgical techniques and results.

CRITERIA OF SUCCESS IN OTOSCLEROSIS SURGERY

In the fenestration operation, attainment of serviceable hearing was the only criterion of success. If the cochlear reserve was such that serviceable hearing could not be attained, the individual was not considered a candidate for surgery.

Initially, the criterion of success for stapes surgery was the same as for the fenestration operation. As time went on the percentage of patients who obtained closure of the bone-air gap through stapes surgery increased, and gap closure rather than serviceable hearing became the major criterion of success. Many individuals who could not be expected to gain serviceable hearing are now advised to have surgery. Some who already have serviceable hearing by the usual

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standards (30-decibel level) are now considered candidates for the stapes operation.

With this new criterion of success, are there many otosclerotic patients who are not candidates for stapes surgery? The answer to this question involves consideration of age, the degree of hearing loss, the amount of bone-air gap, the goals of stapes surgery, unilateral versus bilateral hearing loss, and the diagnosis of far advanced otosclerosis.

AGE

We have no age limits for stapes surgery.

Lower Age Limit. Clinical otosclerosis seldom produces unserviceable hearing under the age of twelve years. If a child under twelve has loss of serviceable hearing with essentially normal bone conduction, lack of progression and no other positive findings of ear pathology, tympanotomy usually reveals ossicular discontinuity or congenital malformation. The child with such a hearing loss is considered a candidate for exploratory tympanotomy as soon as accurate hearing tests can be made.

Upper Age Limit. The upper age limit for stapes surgery is determined by physical rather than chronological age. The oldest patient in our series is 91 years. This patient was young for his age, and fortunately obtained a very satisfactory hearing result.

MINIMAL HEARING LEVEL AND BONE-AIR GAP

Prior to the introduction of various prosthetic techniques, we did not operate on patients with serviceable hearing (30-decibel level), or those who had a bone-air gap of less than 20 decibels averaged in the three speech frequencies. With the techniques currently in use, closure of the bone-air gap to within 10 decibels is obtained in 80 per cent or more of the patients operated. We now perform stapes surgery if the bone-air gap averages more than 12 decibels with at least a 20 decibel gap at one of the three speech hearing frequencies. We rarely operate on a patient whose hearing level is less than 20 decibels (Fig. 2).

GOALS OF STAPES SURGERY

In fenestration surgery, both the surgeon and the patient judged the success of the operation by the same criterion; namely, elimination

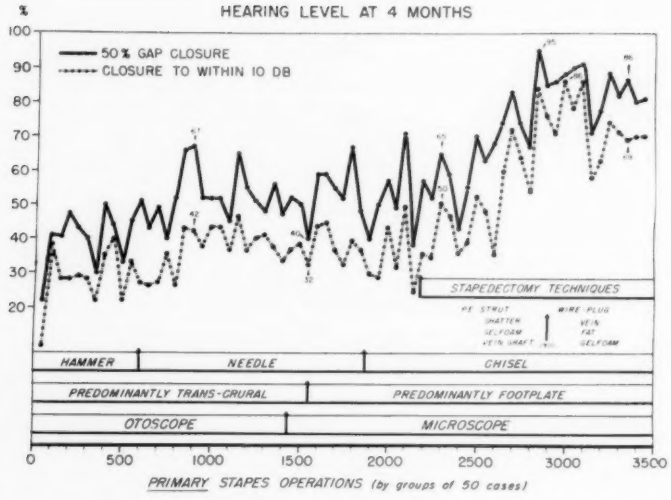

Fig. 1.—Progress graph: Consecutive groups of 50 primary stapes operations showing results at four months relative to technique used.

of the need of a hearing aid. In stapes surgery, it is important that the patient understand the degree of hearing improvement to be expected following surgery. The majority of patients seeking surgery do so with the hope of eliminating the hearing aid and will assume that this will be accomplished. It is most important that the goal of surgery be understood by each patient prior to operation in order to avoid a postoperative disappointment.

The goals of stapes surgery may be divided into four categories:

1. *Essentially Normal Hearing.* For the patient with a bone conduction level of 10 decibels or less, the goal of surgery is to achieve normal hearing.

2. *Serviceable Hearing.* For the patient with a bone conduction level of 15 or 20 decibels, the goal is to achieve serviceable hearing and discard the hearing aid.

3. *Near Serviceable Hearing.* For the patient with a pre-operative bone conduction level of 25 to 30 decibels, the goal is to hear close conversation without an aid. An aid may be needed for distant conversation. Improvement in hearing from the 80-decibel level to

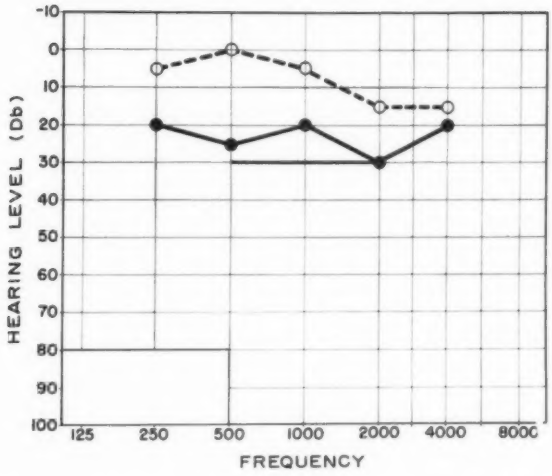

Fig. 2.—"Serviceable" hearing and minimal bone-air gap. Surgery may be indicated in certain individuals with serviceable hearing by the usual standards (30-decibel level), but who none the less are handicapped in their profession. Gap closure should restore normal hearing.

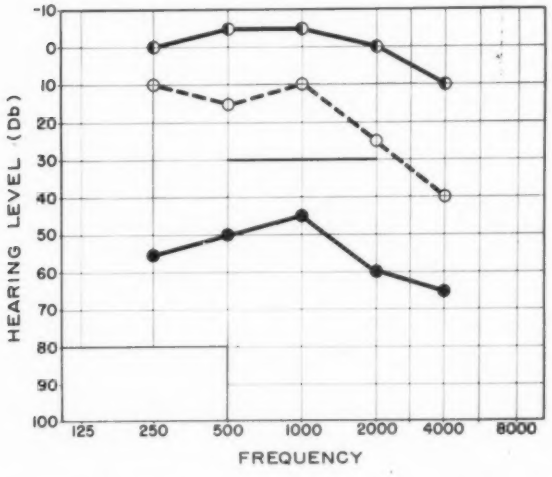

Fig. 3.—Unilateral otosclerosis. Serviceable hearing should result from surgery.

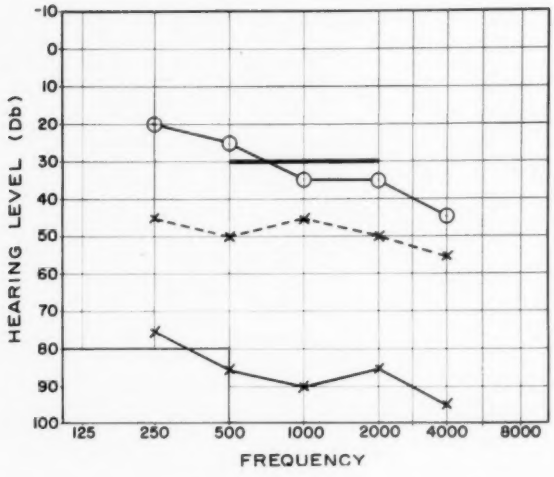

Fig. 4.—Mixed hearing loss due to unilateral otosclerosis with a moderate sensorineural loss in the opposite ear. Successful surgery should allow better use of an aid on the poorer ear.

the 30- or 40-decibel level will allow use of an ear level, rather than a body aid and telephone conversation should be possible without the aid.

4. *Improved Hearing Aid Satisfaction.* For the patient with a bone conduction level of 35 decibels or more, the goal is to obtain better hearing aid satisfaction by converting from a body aid to an ear-level aid in most instances. If surgery is successful, he may be able to hear close conversation without an aid, and be able to use a telephone with an amplifier.

UNILATERAL OTOSCLEROSIS

Binaural hearing has definite advantage over monaural hearing.[4] Localization of sound becomes possible, and the individual can hear conversation on either side. The major advantage, however, is the increased hearing and understanding of conversation in noisy surroundings.

If an individual has normal hearing in one ear, it is questionable whether surgery in the other ear is advisable unless serviceable hearing

can be obtained (Fig. 3). When the ear to be operated is the telephone ear (left ear in a right-handed person), the patient may be happy to obtain an improvement even to the 35- or 40-decibel level providing he has good discrimination.

The individual with a moderate sensorineural hearing loss in one ear and a mixed hearing loss due to otosclerosis in the other often finds it difficult to use an aid satisfactorily in his poorer hearing ear (Fig. 4). The aim of surgery is to improve hearing in this ear to allow better use of an aid. Surgery should not be advised unless the discrimination score is comparable to that of a non-otosclerotic ear and unless the hearing can be improved to within 10 to 15 decibels of this ear.

Regardless of the situation, the advantages to be gained must be understood by the patient prior to surgery, or a successful result from the doctor's viewpoint may be a failure as far as the patient is concerned.

FAR ADVANCED OTOSCLEROSIS

As techniques and results improved, we began to consider the far advanced otosclerotic as a candidate for surgery. This is the individual with a non-measurable bone conduction level and an air conduction level in excess of 85 decibels. The goal in this type of case is to bring the patient from essentially no hearing to some hearing with a hearing aid.

The diagnosis of far advanced otosclerosis in this group of patients is confirmed only by exploratory tympanotomy. The presence of a non-measurable bone-air gap is confirmed only by hearing improvement following stapes surgery.

The following points may be helpful in making a clinical diagnosis of otosclerosis in an individual with far advanced hearing loss:

1. A positive family history is suggestive.
2. The onset occurs in early adult life and the loss is progressive.
3. Paracusis was present in the early stages of the hearing loss.
4. No other cause of hearing loss is apparent.
5. Schwartz's sign may be present.
6. Petrosal sclerosis may be seen on x-ray.[5]

Bone conduction may be measured on the modern audiometer to the 50 or 60 decibel level. The presence of a non-measurable bone conduction threshold better than the air conduction threshold (a non-measurable bone-air gap) is suggested by the following points: 1) the patient usually enters the office wearing a hearing aid; 2) the patient's voice is not suggestive of a purely sensorineural loss (modulation, pronunciation, loudness); 3) the patient may be able to repeat some words or numbers on maximum speech amplification in the test room.

Positive closure of the non-measurable bone-air gap in far advanced otosclerosis is most gratifying. The patient is able to use a hearing aid more satisfactorily due to the threshold improvement and the improvement in useable discrimination.

CONCLUSION

The original criteria for success in surgery for otosclerosis was attainment of serviceable hearing. As our techniques and results have improved, these original criteria have broadened considerably.

Selection of the patient for stapes surgery must include consideration of age, minimum hearing level and bone-air gap, unilateral involvement and far advanced otosclerosis with non-measurable bone conduction. The goals to be obtained in each case must be clearly understood by both the patient and the doctor.

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LXXVIII

TEACHING ESOPHAGEAL SPEECH TO A PRE-OPERATIVE SEVERE STUTTERER

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Since antiquity pathologic stuttering has been a dramatic phenomenon, involving, for example, such prominent personages as Moses, King Charles I, Charles Lamb, and Darwin and having in the United States in our day an incidence of more than one in every 100 individuals. It has also long been the *bete noir* of the speech therapist because of both its bewildering plethora of etiologic theory and a lack of demonstrable therapeutic results. With respect to etiology, Van Riper[1] has observed that lack of a scientific approach to the problem has resulted in sterile research data and has further led to a welter of antagonistic theories whose proponents have spent more time defending their positions than in verifying or disproving them. Among the better known etiologic theories are:

1. The *educational* theory which postulates that stuttering is a fortuitously acquired faulty speech pattern that has become fixated through some continuous emotional force such as fear, ridicule, or feelings of inadequacy.

2. The *analytic* theory which conceives stuttering to be a fixation of the speech mechanism at the oral erotic developmental stage.

3. The *neurological* theory which postulates that stuttering arises from a discordant functioning of paired components of the speech musculature which results from malfunctioning of the thalamus, cerebellum or nondominant cerebrum.

4. The *neurotic* theory which holds that stuttering is the manifestation of a basic personality problem, a maladjustment to the demands of everyday life.

5. The *imagery* theory which attributes stuttering to a lack of visual or auditory imagery.

From the Veterans Administration Center, Bay Pines, Florida.

6. The *inhibitory* theory which postulates that fluent speech is impeded by some *ad hoc* introjected emotional trauma which has conditioned the subject to inhibit certain word cues or elements of the speech situation.

7. The *defensive* theory wherein the stutterer who is asocial, schizoid or paranoid utilizes his disorder as a defensive mechanism which enables him to avoid unwanted social relationships.

Some authorities emphasize the genetic factor in stuttering. For example, Alvarez[2] claims that 25 per cent of stutterers have abnormal electroencephalograms (epileptiform component?) and that 65 per cent of the cases have an hereditary basis. Certain European authorities consider stuttering to be a component, either latent or manifest, of the so-called ixoidian[3] or epileptiform personality. Szondi,[4] for example, delineates stuttering as one of the components of the epileptiform branch of the paroxysmal or hysteriform-epileptiform drive vector, along with asthma, neurodermatitis, migraine, diabetes, syncope and enuresis.

If the interesting theory that stuttering is a paroxysmal epileptiform disorder characterized by tonic, clonic or tonic-clonic spasms of the speech musculature be entertained, it becomes a matter of scientific interest to determine what occurs in the case of a severe stutterer who has undergone a laryngectomy and later mastered esophageal speech. In such a case removal of the larynx, of course, precludes further paroxysmal spasms in that organ. Does the muscular spasm occur elsewhere so that the stutterer nevertheless stutters as an esophageal speaker?

This absorbing question leads one into the area of speech therapy for the stutterer which, to be sure, has gone through many vicissitudes characterized by the use of a variety of mechanical devices and techniques that are ingenious if not necessarily scientific. For example, witchcraft, hypnosis, psychoanalysis, arm swinging, silent finger and toe tapping, and preliminary counting have all been employed as techniques, while the surgeon's scalpel, tongue appliances and the artificial larynx have been among the devices utilized. Through the employment of most of these methods and devices, regardless of how grotesque, "cures" have been reported. In no instance, however, have investigators been able to establish sufficient validity to recommend the procedure or device as a consistently efficacious therapeutic agent.

PARADIGM

This case relates to a 58 year old, white, married, licensed marine engineer who underwent a laryngectomy on August 4, 1960, for a

squamous cell laryngeal carcinoma of the right cord and supraglottic tissues posteriorly. He ceased working in 1945 because of "nerves and back." For this condition he receives veterans' compensation and carries a diagnosis of "psychoneurosis and situational back injury." He also complains of continual headaches which he thinks are "due to nerves." He states that in the past he has been treated with narcotics to attain relaxation, but he adds that he can secure as much relaxation from a drink and, further, that he can "give up the drinking, but not the dope." He holds a marine engineer's license but, nevertheless, has been able to make only one trip to sea because of inability to concentrate on his duties.

As revealed clinically and confirmed by tape recording, his stuttering was so severe as to render the subject almost incapable of communication. Regarding the history of his stuttering, he related the following: "It started about 15 years ago. The doctor said it was caused from my nerves and shock from an accident. Sometimes it's not so good and sometimes it's better (paroxysmal). It is better if I don't get excited over it, but it has been getting worse all the time and is much worse lately. The thing that helps me most is a drink of whisky."

His narration was accompanied by marked emotional stress and from time to time he was too tearful to proceed. There was no evidence, however, of anomia, perseveration of thinking or other encephalitic or encephalopathic signs, nor of automatic phrasing in speaking, lack of hand-eye co-ordination or emotional blocking in handwriting.

PREVIOUS STUDIES

Since this was the speech therapist's first experience with a preoperative stutterer and only one analogous case could be found in the literature,* he communicated with 34 authorities in the field of neur-

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* C. Van Ripper quotes (Speech Therapy, Prentice-Hall, Inc., New York, 1953, p. 111) from an article by V. O. Mabel Oswald entitled "Oesophageal Voice Following Total Laryngectomy," *Report of the Conference on Speech Therapy*, 1948, p. 94, that a Miss Oldrey had such a case and reported that:

> "The first week when we were trying to get the sound, it was very difficult, but as the man is learning to use the esophageal voice the stammer is disappearing. He is 58, has stammered all his life and never had any treatment for it."

Curiously enough, in a recent communication from Hampshire, England, to one of the authors, V. O. Mabel Oswald disclaims knowledge of the case and states emphatically, "I have never dealt with a combination of these two difficulties (stuttering and laryngectomy) in one patient nor written about it!" She then adds, however, "I am pretty certain that your patient will *not* stammer (or stutter) subsequently."

ology, otolaryngology, psychology and speech pathology in the United States and six foreign countries. To these individuals he addressed the following questions:

1. Will a laryngectomee who severely stuttered pre-operatively continue to stutter after he becomes an esophageal speaker?

2. Have you personally known or had experience with a pre-operative stutterer who later became an esophageal speaker?

3. Have you read or noted references to such a case in the professional literature?

In every instance the addressee responded. The results were as follows:**

	Number	*Per cent*
QUESTION 1		
a. Will stutter	5	14.7
b. Will not stutter	4	11.8
c. Unwilling to conjecture	24	70.6
d. Depends on the individual	1	2.9
Total	34	100.0
QUESTION 2		
a. Never knew or had personal experience with such a case	34	100.0
QUESTION 3		
a. Have neither heard of nor seen any reference in the literature to such a case	30	88.8
b. Was informed of, or have seen a reference to such a case	4	11.2
Total	34	100.0

**Further details regarding the authors of these communications or the subject-matter thereof are available on request.

The comments of the b. group of Question 3 were interesting. They were as follows:

1) "The only laryngectomee I ever knew who was a stutterer was an inmate of the ..... Penitentiary. So far as I know he never mastered the art (esophageal speech) after he had made a bit of progress."

2) "Two laryngectomee cases were former stutterers. Both developed excellent esophageal voice with no evidence of stuttering."

3) "I know of two cases of stutterers who had laryngectomies, one of whom stuttered postoperatively and the other did not. . . . I am not aware of any literature on this subject."

4) "From colleagues . . . I get the information that one laryngectomee (who was a pre-operative stutterer) continues to stutter occasionally. . . . I, myself, have never had any experience with such a case. . . . I have had several students search the medical and speech pathology literature for the past sixty years but they could come up with nothing."

It will be noted from the above data that such cases are unusual and of a type not found in the literature.

PERSONALITY STUDY

Purpose. In order to glean data relating to pre-operative and postoperative aspects of the subject's personality, a depth psychologic longitudinal study was undertaken. The purpose of this study was threefold, namely:

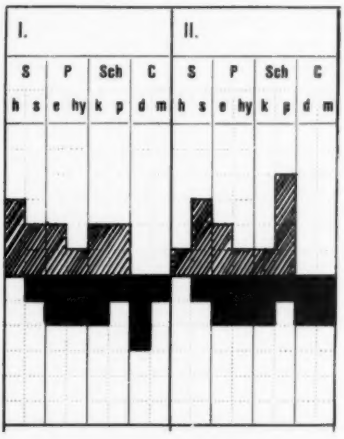
a. To gain information relative to the salient personality traits of an individual who had developed laryngeal carcinoma realizing, of course, that this personality pattern would not necessarily be typical of the group as a whole. Such a special group, however, is now under study.

b. To determine whether a noteworthy personality change occurs as a result of surgery which deprives the individual of a vital expressive organ—vocal speech.

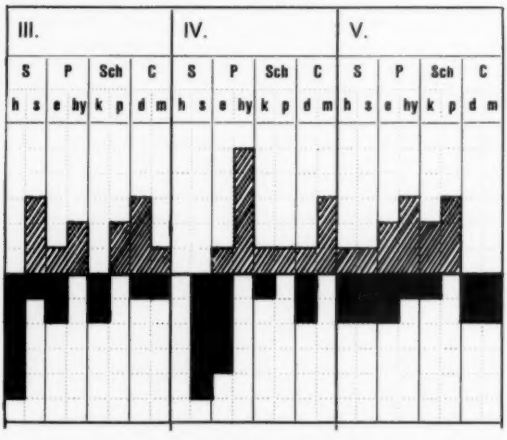
c. To provide knowledge of the subject's personality which would be helpful in the planning and conduct of esophageal speech instruction.

To attain these objectives the Szondi test[5] was utilized both because of the prominence of the Szondian theory of stuttering and the fact that the test is longitudinal yet devoid of practice effect.

PRE-OPERATIVE AND POSTOPERATIVE SZONDI PROFILES OF A LARYNGECTOMIZED PRE-OPERATIVE SEVERE STUTTERER



Pre-operative Profiles



Postoperative Profiles

Figure 1

SZONDIAN FOREGROUND STRUCTURAL ANALYSIS

195		S		P		Sch		C		Σ	Σ	Σ
1960	Nr.	h	s	e	hy	k	p	d	m	0	±	0& ±
7/28	I	+	+	±	-	±	+	-	0	1	2	3
8/3	II	0	+	±	-	-	+!	-	-*	1	1	2
8/15	III	-!!	+	-	+	-	+	+	0	1	0	1
8/22	IV	0	-!!	-!	+!!	0	0	-	+	3	0	3
8/24	V	-	-	±	+	+	+	-	-	0	1	1
	VI											
	VII			*Murderer's E								
	VIII											
	IX											
	X											
Σ 0		2	0	0	0	1	1	0	2	6		
Σ ±		0	0	3	0	1	0	0	0		4	
Tendency tension		2	0	3	0	2	1	0	2			10
Degree of latency		S -	2	P -	3	Sch -	1	C -	2			
Quantity of tension		h	s	e	hy	k	p	d	m	Σ:		
		2	2	1	2	0	1	0	0		8	

Drive Class: $\frac{P^{hy}+}{3}$ $\frac{S^{s}+}{2}$ $\frac{C^{d}-}{2}$ $\frac{Sch^{p}+}{1}$ $\Sigma ! = 8$

Quotient of Tendency Tension: $\frac{\Sigma 0 \quad 6}{\Sigma \pm \quad 4} = 1.5$

% Symptom Reactions: 25 Waltisbuehl Social Index: 36

Drive Formula:

$$\frac{e}{\begin{matrix} h & k & m \\ p & s & hy & d \end{matrix}}$$

Figure 2

Five profiles were secured with a period of one week intervening between successive profiles. Two of these profiles were secured preoperatively and three postoperatively. A blind analysis of the profiles was accomplished by one of the authors,[6] that is, without knowledge of the individual's past history, following which the findings were collated with and confirmed by anamnesis. The profiles are reproduced as Figures 1 and 2.

ANALYSIS

Profile I (pre-operative) indicates an individual who utilizes compulsive activity as a means of repressing his tendency toward paranoid suspicion and distrust, a desire for self-concealment and an asocial attitude toward people. These traits emanate from a tendency to accumulate in the background facet of the personality the gross effects of rage, anger, vengeance, hatred, jealousy and envy. On the other hand, the subject has a firm, loyal and dependent bond to the primary love object, who apparently is his wife. Toward others he is quite passive, effeminate, deferent and self-effacing. He is inclined, moreover, to become easily discouraged.

Profile II (pre-operative) indicates an individual who is becoming more aggressive, but who still is able to inhibit overt aggressive behavior. There has developed at this point, however, an accumulation of the gross effects of rage, anger, hatred, vengeance, jealousy and envy. The tendency toward self-effacement continues, but the bond toward the favorite love object has weakened.

Profile III (postoperative) reveals a marked change. Here the subject revelas a complete repression of all amorous tendencies with perhaps a tendency to turn more toward masculine than feminine types of emotional attachment. The gross effects are now dangerously near an overt expression and are inhibited only with considerable effort by an ego which has completely lost its cathexis to love objects and succumbed to an egocentric need to live only for the satiation of the individual's own needs.

Profile IV (postoperative) depicts a reversal of the subject's aggressive tendencies to masochistic ones. There is a very strong self-punitive tendency which, coupled with excessively accumulated gross effects directed against the self, an egocentric attitude toward others, an impotent judgment and a lack of mental control, constitutes a suicide potential. The profile indicates clearly that the individual is in a serious personal crisis, which is apparently a delayed emotional reaction to his operation, which he now conceives as a mutilation.

Profile V (postoperative), which is the final one, discloses an individual who is estranged from intimate human relationships. His aversion to and renunciation of amorous objects and his efforts to restrain his gross effects from expression have created a very tense ego. He, accordingly, is compelled to exert a maximum effort to maintain a semblance of mental control.

Taking the profiles as a whole, one notes the so-called open Murderer's E of foreground Profile V, the Murderer's E in *theoretic* complementary Profile I and in Profiles II, III and V of the *empiric* complementary background. These pathognomonic constellations reveal the epileptiform or ixoidian personality which contemplates a paroxysmal disorder, such as the stuttering and the propensity to follow a peripatetic occupation which is related to heights, water or depths and characterized, of course, by his vocation of marine engineer. The excessive loading in factors, h, s, e, and hy reveal an accumulated tension resulting from an inhibition of the gross effects above mentioned. The drive formula with its greatest manifest expression in the drive factor e (epileptiform), the fluctuations of the — and ± reactions in this factor and the chief drive class depicted in the paroxysmal vector all portray the volatile hystero-epileptiform behavior which will inevitably characterize this individual. Moreover, the fluctuation between the urge for self-display and self-concealment which the weak ego is unable to mediate, as indicated by the k factor's vacillatory behavior, will all result in heightened sensitivity, inconsistent overt behavior and, consequently, poor adjustment in a class situation. Likewise, the tendency to remain loyally attached to cherished personal objects or to become detached from them, as reflected by the alternation of the 0, — and + reactions in the m factor, accounts for this individual's ambivalent behavior toward others, an ambivalence which is rooted in an innate confusion in his proper sex role and manifested chiefly in an ambivalence between aggressivity and passivity. This ambivalence the subject will doubtless exhibit toward the speech instructor as well as other people. Finally, should be mentioned the social index of 36, which ranks below the minimum of 40 indicative of the normal individual and which, accordingly, represents asocial characterological traits.

In summary, then, one can characterize this individual as tense, unstable and asocial. Alternately he will exhibit hostility toward others and turn the aggression against himself through self-punitive or masochistic behavior. The paroxysmal syndrome is clearly portrayed in the test data and delineates the subject as an ixoidian who thus is embraced within the category of innate stutterers as well as within a group in which there occurs substuperous states and potential suicide risk. It is not, therefore, difficult to discern that he not only will have difficulty in adjusting to his laryngectomy, but also in consistently maintaining the necessary conformity and docility to render speech instruction feasible. Considerable patience, tact, attention and individual instruction will be required in order for this individual to master esophageal speech.

INSTRUCTIONAL GOALS AND METHODOLOGY

The goal set for this case was a fluent expressive speech without facial contortions or other mannerisms and accompanied by such a degree of self-confidence as would preclude a relapse into stuttering. Since examination indicated that all speech molds were present, these goals seemed feasible.

In order to establish rapport, pre-operative visits were instituted and following surgery a continuing contact was maintained with the patient.

Following postoperative recovery, esophageal speech instruction was instituted in a class comprising the subject and three other students. It became immediately apparent, however, that instruction would have to be individualized. When patient observed the other students performing in class, he became discouraged and tearful and expressed threats of self-destruction if unable to speak again and without stuttering. He frequently expressed serious doubt that he would ever be able to speak again and continually negated constructive suggestions by a vigorous shaking of the head. Following 46 hours of instruction, however, most of which comprised individualized instruction, he did master esophageal speech and was able to participate in an extended fluent conversation which was recorded and determined to be free of pathologic stuttering.

CONCLUSION

This report involves a 58 year old pre-operative severe stutterer who underwent a laryngectomy for laryngeal carcinoma and who afterwards was taught esophageal speech. The goal was to develop a fluent speech and sufficient self-confidence to make it a permanent tool of adequate expression. Depth psychological Szondi profiles seemed to confirm the Szondian theory that stuttering is a paroxysmal disorder which is a component of the ixoidian personality in the Strømgen sense,[1] since the epileptiform syndrome was clearly inherent in the test profiles secured and was manifested in the emotionally unstable behavior of the subject in the class situation. Nevertheless, by virtue of individualized instruction accompanied by generous emotional support, the patient was able to develop an esophageal speech which was fluent and free from pathologic stuttering. Three months later the stuttering had not returned. Whether this esophageal speech will remain free from the effects of stuttering with the

further passage of time and will further endure the stress of life exigencies cannot, however, be yet inferred.

VETERANS ADMINISTRATION CENTER

Mr. Irving is speech therapist, and Dr. Webb is chief psychologist at Veterans Administration Center, Bay Pines, Florida.

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LXXIX

A DISCUSSION OF FORTY-TWO YEARS' EXPERIENCE WITH OTOLARYNGOLOGICAL PATHOLOGY

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I am giving this talk because I feel a great sense of personal obligation to the specialty of otolaryngology and this will be the general theme I will follow. When I took my assignment in 1919, I visualized a new horizon of pathology. I had been teaching general pathology for years in medical schools. When I was offered this position, little did I know what might happen in the years to come, because like most general pathologists, I was little interested in nor familiar with the pathology of otolaryngology and particularly of the neoplastic diseases.

I will discuss some cases of papillomatosis or chronic papillary sinusitis. In 1854, Billroth[5] considered polypi in the nose to be myxomatous tumors. Later he believed that all nasal polyps were adenomatous. This was refuted by Hopmann,[17] who described a number of proven papillomata that had been confused with the polypi. Permit me a word: A polyp consists of edematous connective tissue stroma. Papilloma consists of marked hyperplasia of surface epithelium. Doctors still, in error, refer to a papillomatous lesion as a polypoid lesion.

In 1895, Wright[39] explicitly set forth the distinction between polypi and papillomata. In 1908 he reported two cases which simulated malignant lesions. Others reported similar cases, notably Kiesselbach[18] and Arrowsmith.[1] Dr. Jonathan Wright[39] did much for otolaryngology. I recommend to otolaryngologists to read all of his books and, in particular, his History of Otolaryngology, published in 1914. In 1886, Verneuil[37] reported benign papillomata that had recurred in spite of several removals. In 1897, Hellmann[15] wrote upon the nasal papillomata and their transformation into carcinomata.

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Read at the meeting of the American Laryngological Association, May 22, 1961.

Dr. Ewing[12] reported a case of nasal papilloma that recurred after removal, for ten years, and eventually became carcinomatous. To Hopmann belongs the original observation of soft papillomata of the nose and sinuses and the lesions have been referred to as Hopmann's sinusitis. Hopmann's observations received support from many other confreres of his time, namely, Mackenzie,[26] Chiari,[7] Wright[39] and recently by Eggston and Wolff[11] and Ash and Baum.[2]

I see a goodly number of cases of papillomatosis annually, but not nearly as many as polypoid cases. At all times, tissues surgically removed should be analyzed microscopically. Respiratory epithelium in the upper and lower respiratory tract can and does undergo extensive metaplasia due to prolonged infection or irritation, such as smoking. Such a change may be the forerunner of malignancy.

Presentation of my cases will be in abstract.

PAPILLOMATOSIS

Various types of papillomatous changes are shown in Figure 1. Some cases of benign nasal papillomatosis have come to my observation where radical operations were recommended to which I could not agree. Such benign cases had simple exenteration of the diseased sinus mucosa, without further recurrence. If the papilloma has degenerated into a carcinoma, then, of course, early radical operation should be done.

The first case is of benign papilloma where simple exenteration of the lesion sufficed. The patient is still in good health after five years. A radical operation had been advised, but not done (Figs. 2 and 3).

Next is the case of an otolaryngologist who suffered for years with sinusitis, which terminated in carcinoma. From 1936 to 1941 he was treated for an allergic sinus condition. In 1941 a thorough investigation of the sinuses revealed a marked thickening of the mucous membrane in the left antrum, with a diagnosis of chronic maxillary sinusitis. He preferred occasional washings, which were done intermittently from 1938 until 1954. Repeat x-rays in 1954 revealed the same pathology of the antrum. An exploratory antrotomy was performed in October of 1954 which confirmed the diseased mucous membrane. In the removal of the membrane, the surgeon found a small bony dehiscence, 2 mm in diameter, and suspected a malignancy. A biopsy was done from the antrum and because of several different opinions by several pathologists, in January of 1955

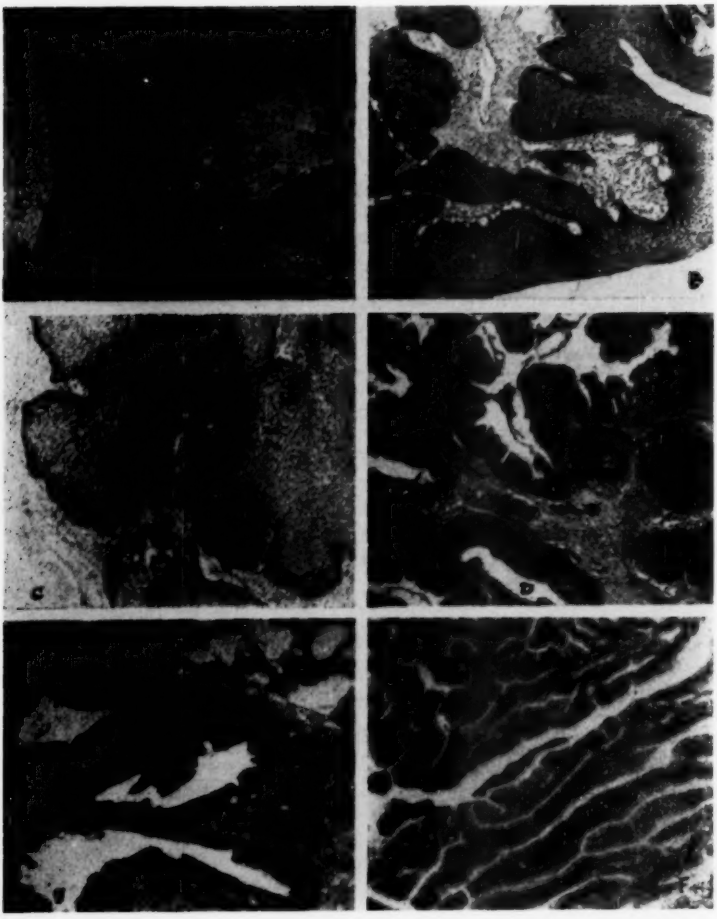

Fig. 1.—Papillary sinusitis (from Eggston and Wolff[11]). A. Normal and metaplastic epithelium. Hydropic degeneration of cells. B. Metaplastic epithelium. C. Papillary sinusitis of the ethmoid, epidermoid type. D. Papillary sinusitis of the ethmoid, foliate type. E. Papillary sinusitis of the ethmoid, cryptic type. F. Papillary sinusitis of the antrum, filiform type. Erroneously called "nasal" adenoma.

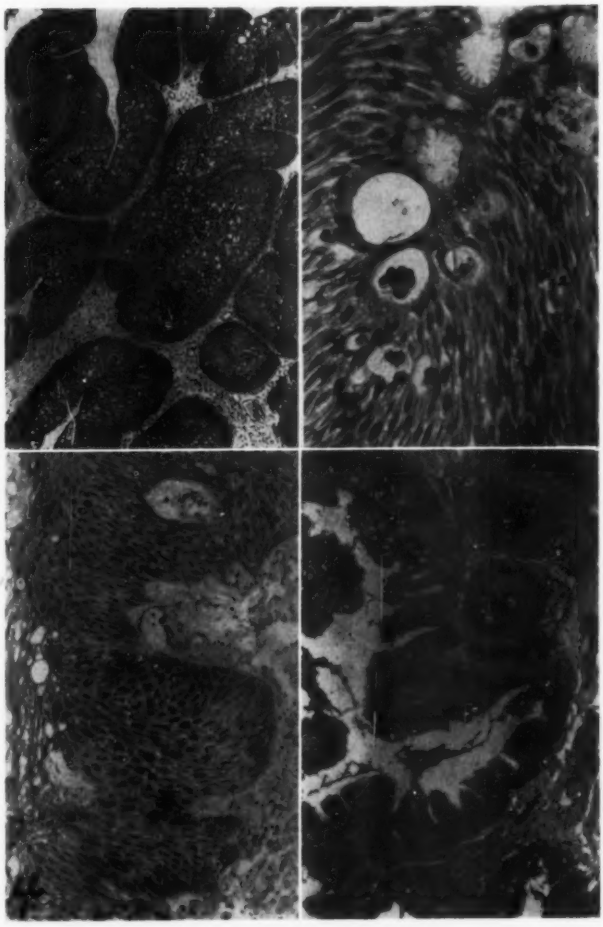

Fig. 2.—Squamous cell type of papillomatosis.

Fig. 3.—Higher magnification of an area from Figure 2 which illustrates in detail the squamous cell type of lesion, vacuoles containing leukocytes (1) and clear halo around some of the nuclei (2), suggestive of virus disease.

Fig. 4.—Carcinoma in situ, of antrum.

Fig. 5.—Metaplasia of the epithelium with areas suggestive of early carcinoma.

the patient was rebiopsied, followed by a similar difference of opinion by pathologists. However, a positive diagnosis of epidermoid carcinoma was agreed upon. Since surgery would necessarily have to be very radical, the patient elected x-ray therapy and received 5600 r.u. without improvement. The disease progressed until October 1955, when it was evident that there was extension of the process. The patient refused further x-ray treatment. He finally accepted radical surgery. This was done in October 1955, with radical maxillectomy and exenteration of the orbit. The patient ran the usual postoperative course and did very well until April when his discomfort became severe. In September, repeated biopsies revealed carcinoma. The patient desired no further surgery, so further x-ray was instituted, without relief. The disease continued to spread for 18 months before his demise, from extensive epidermoid carcinomatosis (Figs. 5, 6, 7). At times, the malignancy starts as carcinoma in situ (Fig. 4).

The next case of papillomatosis is of Mrs. K. This 56 year old woman had protracted sinusitis for years. Finally a biopsy revealed an epidermoid carcinoma. Radical surgery and radiation were given with no avail. The patient lived one year and died of carcinomatosis (Figs. 8 and 9).

NON-CHROMAFFIN PARAGANGLIOMA, GLOMUS TUMOR, GLOMUS JUGULARE, CHEMODECTOMA, ETC.

This presentation includes the glomus tumor group. There are recorded in medical literature as many as 20 synonyms of tumors of the carotid body and other structures. In 1950, Mulligan[28] used the word "chemodectoma" to describe the glomus tumors. Such designation does not completely satisfy many pathologists. It does not assay the histogenesis and complete physiology of glomus tumors (Boyd,[6] Smith[34]). These ganglion structures are probably chemoreceptors as well as chemodectors and receive chemical stimuli which are transmitted to the central nervous system. It is postulated that the changes in electrolytes, CO_2, sodium, potassium, calcium and oxygen tension have some relationship to the function of these structures. There are numerous locations where paraganglion cells and glomus tumors occur, namely in the carotid body, jugular bulb, the nodosa ganglion of the vagus nerve, ganglia of the glossopharyngeal nerve and tympanic nerves, also the aortic[22] and coccygeal bodies and minute pulmonary bodies. Philip M. LeCompte[24,25] published a complete review of the tumors of the carotid body and related structures as a section of the Atlas of Tumor Pathology in 1951, published by the Armed Forces Institute of Pathology. Costero[8] et al. demonstrated morphologic

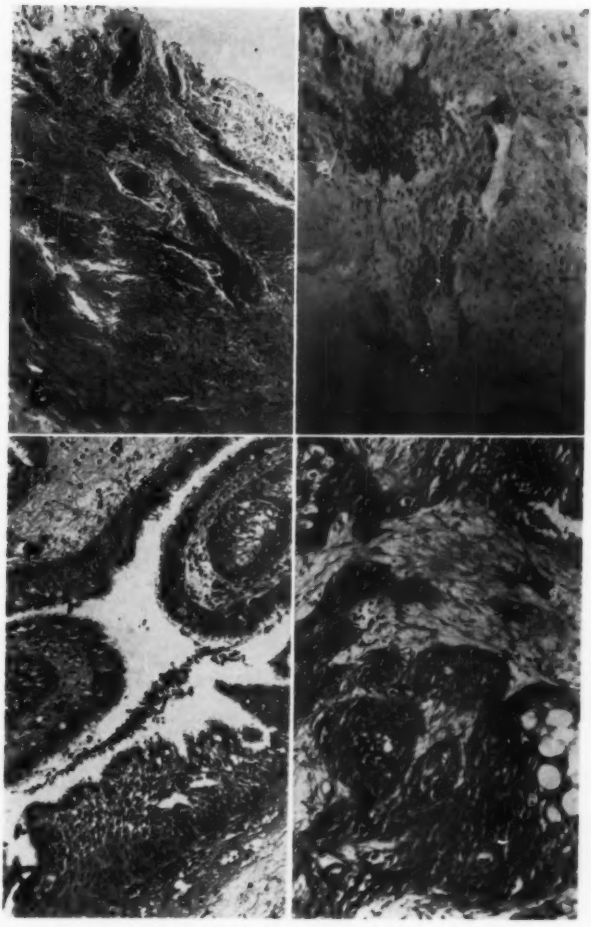

Fig. 6.—Areas (1) showing epidermoid carcinoma.
Fig. 7.—Areas of epidermoid carcinoma.
Fig. 8.—Foliate type of sinusitis areas (1), metaplasia.
Fig. 9.—Anaplastic epidermoid carcinoma. Grade IV.

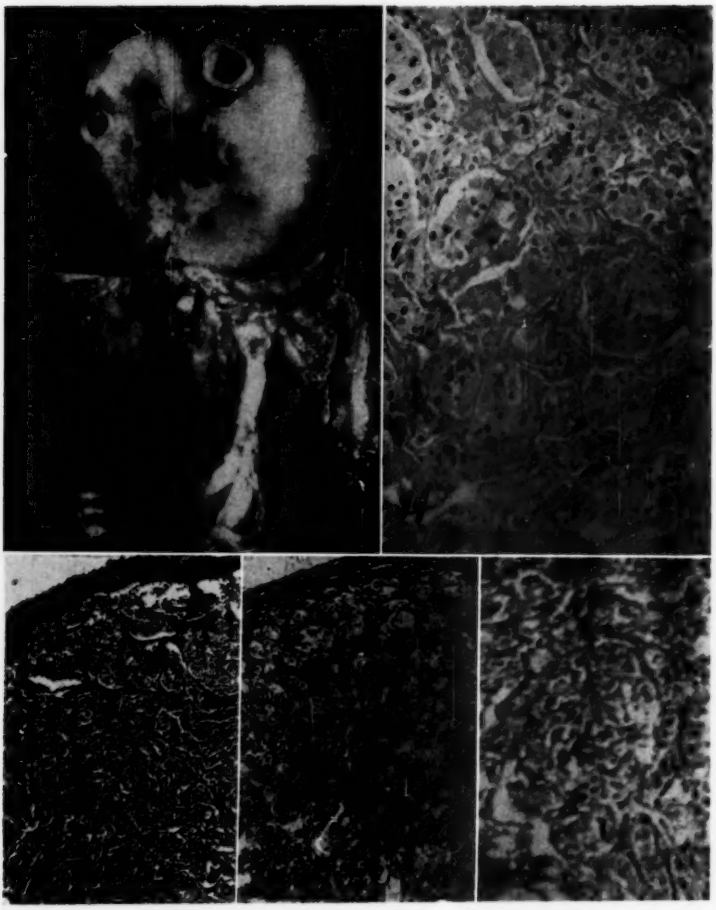

Fig. 10.—Carotid body tumor, surrounding the carotid arteries.

Fig. 11.—Microscopic structure of Figure 10, revealing "Zellballen of chief cells.

Fig. 12.—Glomus tumor, middle ear (x 58), "Zellballen" (1).

Fig. 13.—Same as Figures 12 and 14.

Fig. 14.—Glomus tumor, middle ear (x 100). Higher magnification of (1), Figure 12.

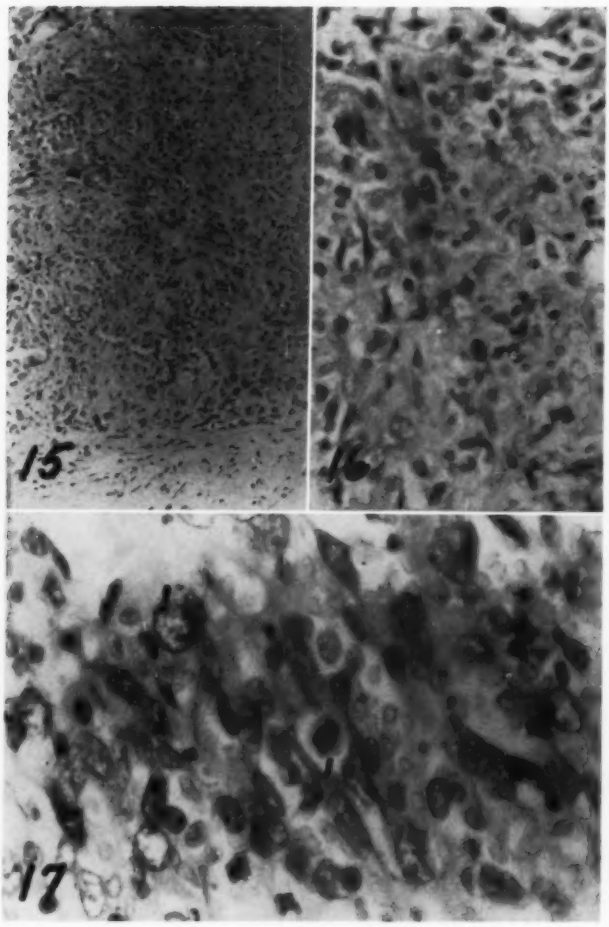

Fig. 15.—Malignant carotid body tumor, (x 60).

Fig. 16.—Malignant carotid body tumor, (x 100).

Fig. 17.—Malignant carotid body tumor, (x 200) showing chief cells and mitosis.

properties with nerve and vascular connections to the chief cells of glomus tumors.

The first case is of a woman operated upon in 1943 when 40 years of age. After 18 years, she remains in good health. Dr. Nigro resected the tumor which surrounded the carotid arteries. There were no central nervous system symptoms following the operation because the carotid arteries were constricted. In many cases the vessels are surrounded by tumor which makes complete resection hazardous (Figs. 10, 11).

The second case was seen by Dr. Wolcott in May of 1955. The patient had a progressive deafness and pain in the left ear with deep-seated headache and unsteadiness. About a year previously, she consulted another otologist who made a diagnosis of a polyp, which he attempted to remove. This was followed by severe bleeding, necessitating hospitalization and transfusions. There is no record of a microscopic examination done at that time. When examined by Dr. Wolcott, there was, in addition to pain, instability and considerable loss of hearing, also hoarseness. Examination revealed a large fleshy-looking polyp. It filled the external auditory canal, with reduction in hearing, and paralysis of the left vocal cord was present. X-ray revealed an invasive lesion involving the base of the skull and obliteration of the middle ear anatomy. Biopsy was taken by electric snare, followed by considerable bleeding. Microscopic examination revealed a non-chromaffin paraganglioma which was considered inoperable and was treated by x-ray therapy. She first received 2000 r.u. with little improvement, and in 1955 she was given a second course of x-ray treatment which was followed by marked improvement. The lesion in the ear disappeared, although her vocal cord paralysis remained. In April of 1961, she was examined, without evidence of recurrence. Her general health was good, she was only slightly unsteady. However, the paralysis of the vocal cord remained (Figs. 12, 13, 14).

The third case of glomus tumor, E.L., has been previously reported clinically by Dr. F. M. Turnbull.[36] I wish to report a more detailed pathological finding in this case. The patient was a white male, 48 years of age, admitted to the Hospital in January, 1952, with a tumor mass in the right upper neck, of 10 years' duration. The mass slowly increased in size, with pain for the past two months. In July 1951, a biopsy was taken and reported as a carotid body tumor. Examination in our Tumor Clinic revealed a tumor mass measuring 9 x 6 cm in the right upper third of the neck and encroaching upon the mandible. The mass was not tender and there was no pulsation. It was rubbery and slightly movable, vertically. Biopsy on January

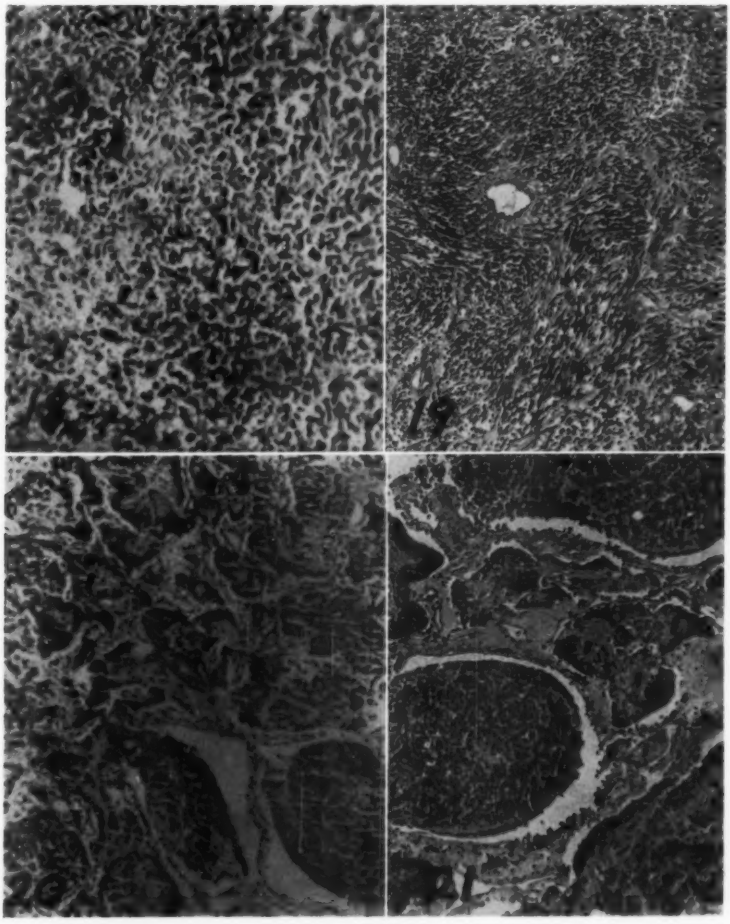

Fig. 18.—Nasopharyngeal tumor, Pt. L, three years, diagnosed as neuroblastoma. (See Figure 19.)

Fig. 19.—Cervical lymph node metastasis, Pt. L, three and one-half years. Diagnosis: rhabdomyosarcoma.

Fig. 20.—Neuroblastoma (Esthesioneuroepithelioma) of antrum, revealing pseudo-rosettes.

Fig. 21.—Neuroblastoma (Esthesioneuroepithelioma), higher magnification of pseudo-rosettes. Note loose fibrous material in central core.

23 was reported as a carotid body tumor with sarcomatous changes. A right radical neck dissection was performed and the tumor removed. It was encapsulated and firm and intimately adherent to the carotid vessel and the vagus nerve. External and internal carotid arteries were enveloped by the mass. The lumen of the internal carotid artery was occluded. Pathological examination revealed a sarcoma of the carotid body, confirmed by several pathologists, with comments that they had never seen a malignancy of carotid body tumors. Sections revealed a pleomorphic cellular mass, chiefly spindle cells. The operation was done in January. In March 1950, the patient returned with a 2 cm tender mass beneath the mastoid process and behind the cervical scar. Another mass was found in the right submental area. He had pain and loss of weight. These recurrences were resected and found of similar histology as the primary tumor. In July 1950, x-ray of the chest revealed metastatic lesions throughout the lungs. The patient was discharged for terminal care. He expired in August of 1952. Autopsy revealed generalized metastasis with extensive involvement of the lung. This case illustrates that if carotid body tumors are allowed to run their own course, a significant number will eventually become malignant (Figs. 15, 16, 17).

NEUROBLASTOMA, ESTHESIONEUROEPITHELIOMA OR NEUROCYTOMA, ETC.

There are nasopharyngeal tumors that are diagnosed as neuroblastomas, reticulum cell sarcoma, lymphoma, Hodgkin's disease, fibrosarcoma, angiosarcoma, rhabdomyosarcoma and simply as highly anaplastic tumors. Regardless, the course and ultimate outcome is very discouraging as most of these cases are fatal in the young. Salas[31] reported 16 cases in ages between one and three years who lived from two weeks to eight months. I confess to errors in the pathologic diagnosis in this tumor category.

The first case is of a three year old Puerto Rican girl, presenting a tumor mass in the nasopharynx, at first diagnosed as a fibrosarcoma or neuroblastoma. Later on there was cervical lymph node metastasis. Examination revealed that this was a rhabdomyosarcoma. The patient received extensive radiation. However, within less than a year there was generalized metastasis and the patient expired (Figs. 18, 19).

The second case I wish to present briefly is H.K., a white female, 33 years of age, who was admitted August 1953 and was operated upon for a malignant neuroblastoma of the left antrum. There was a palpable swelling of the left antrum and a bulging mass in the left

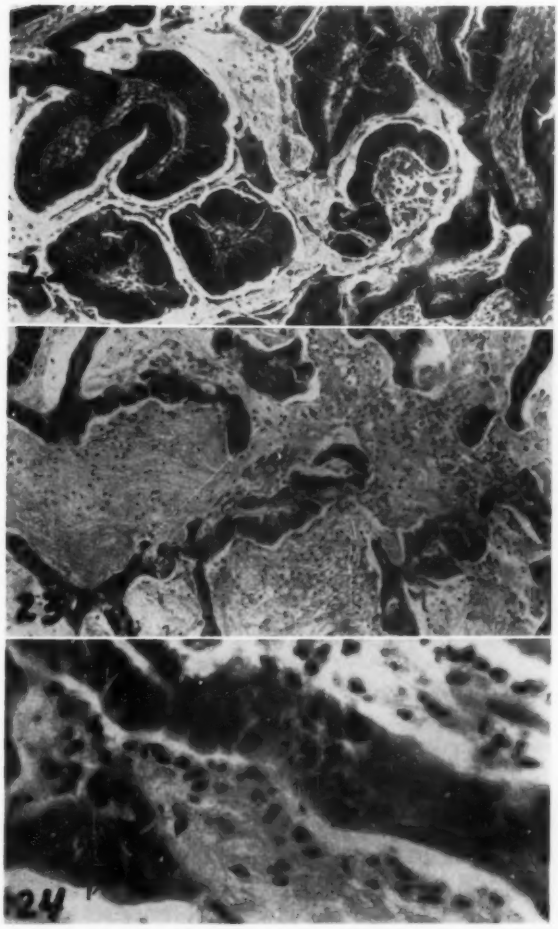

Fig. 22.—Papillary neuroepithelioma (Esthesioneuroepithelioma), (x 100), revealing strands and areas of tall columnar olfactory nerve sensory receptive cells. Some of the cells have hair-like processes on the external borders.

Fig. 23.—Higher magnification of similar trabeculae of olfactory nerve cells.

Fig. 24.—Higher magnification of columnar cells revealing anisocytosis, hyperchromasia and mitosis (1).

nares. There was also a mass in the left buccal fold with a dehiscence of the right palate. Biopsy revealed a malignant neuroblastoma. X-ray revealed bony destruction of the left antrum and the left upper antral plate. There was a radical left maxillectomy with exenteration of the left orbit, also the ethmoid, sphenoid and ptergoid fossa were removed. The operation was performed September 4, 1953. On January 2, 1954, there was a recurrence. The patient received x-ray tratments in 1954, of 5000 r. u., with marked improvement. After this the patient returned to the Tumor Clinic in 1954 and yearly until April 5, 1961, without any evidence of recurrence. McCormick and Harris[27] reported four similar cases which they preferred to call neurocytoma. Schall[32] reported primary intranasal neuroblastoma. Others have reported similar cases (Figs. 20, 21).

The third case is of N.F., white male, 69 years of age. He was admitted to the Hospital March 14, 1957, because of difficulty in nasal breathing. A biopsy revealed a papillary neuroepithelioma.[11] X-ray examination revealed four-plus involvement of the right ethmoid and antrum and two-plus of the right sphenoid. The patient was referred for radiotherapy in January 1957, by the tumor clinic, but it was thought that the tumor was radioresistant. A total dose of 5500 r.u. was given without appreciable change in the patient's condition. Patient was operated upon February 14, 1958. There was a right maxillary resection and a right orbital exenteration. On June 27, 1958, there was a recurrence of the tumor and a wide local excision was done. On March 12, 1959, the patient was re-operated upon for a recurrence and a right radical neck dissection was done. Patient returned several times in 1959 and 1960 without any evidence of recurrence. The last visit was in March 1961, without evidence of recurrence.

Frühling and Wild[13] report four cases of neuroblastoma olfactory esthesioneuroepithelioma similar to those reported by Louis Berger.[4] These types of tumors have received a great deal more attention in Europe than in this country, particularly in France. They report the clinical symptoms and histology in detail, particularly the true rosettes and neurospongial cells. They speak of the attenuated malignancies, as they are extremely sensitive to surgical and radiation treatment, resulting usually in cure, as were the two cases above reported (Figs. 22, 23, 24).

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Scientific Papers of the American Broncho-Esophagological Association

LXXX

SUBGLOTTIC HEMANGIOMA AS A CAUSE OF RESPIRATORY OBSTRUCTION IN INFANTS

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Hemangioma is an extremely common congenital abnormality of infants. During a period of 20 years from 1936 to 1956 at the Children's Hospital Medical Center in Boston, MacCollum and Martin[1] reported on 6479 patients with hemangioma seen by the Department of Plastic Surgery. Cutaneous hemangiomas associated with those of other organs have led to the establishment of various specific eponymic syndromes, such as Jaffé's syndrome (hemangiomas of skin and abdominal viscera); Kast, or Maffucci syndrome (hemangiomas of skin and enchondroma of bone); Sturge-Weber, or Cushing, syndrome (hemangiomas of skin and central nervous system or meninges); and von Hippel-Lindau syndrome (hemangiomas of retina, central nervous system and viscera). Only in recent years has attention been drawn to the association of hemangiomas of the skin with a similar lesion in the subglottic region. Hemangioma of the subglottic area should always be considered in any infant with laryngeal stridor or respiratory obstruction, regardless of the duration or constancy of the symptoms. So far as we know, as yet no proper name has been attached to this latter syndrome.

In an infant with an extensive hemangioma of the face and neck, there is always the possibility that the lesion may involve the larynx as well as other adjacent regions. Baker and Pennington[2] have given an excellent report of such cases. However, a localized sub-

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glottic hemangioma often occurs when a cutaneous lesion is either absent or very insignificant. Under these circumstances the presence of such a tumor in an infant with stridor or high airway obstruction is often unsuspected, and apparently too frequently discovered only by postmortem examination. The episodic nature of the symptoms, often mistaken for "croup," is characteristic of subglottic hemangioma, and is thought to be due to varying degrees of vascular engorgement of the tumor.

During the 10 years from 1951 through 1960 at the Children's Hospital Medical Center in Boston, the Department of Otolaryngology has seen and treated 17 infants with subglottic hemangioma. Each patient was diagnosed and treated with satisfactory results, in all but one instance. Throughout this period the Department of Pathology had performed no postmortem examination in which a subglottic hemangioma was found (except in the one fatal case which had already been accurately diagnosed and properly treated). In every postmortem examination it is the policy of the pathologists to examine very carefully the organs of the neck, and histologic sections are always taken through the thyroid and lower laryngeal regions.

A review of the literature reveals a very different record. Fifty per cent of the reported cases of subglottic hemangioma were fatal, and in 9 out of a total of 24 patients, the proper diagnosis was unsuspected, and made only at autopsy. In only 15 patients was the lesion recognized during life, and 3 of this group later succumbed to pulmonary complications. In 1958 Doermann et al.[3] in a report of a fatal case of subglottic hemangioma, listed the pertinent findings in the 14 case-histories already collected from the literature, and added their own. Since then we have found 9 more such case-reports, and have added them in the following tabulation (Table I).

SEX AND AGE INCIDENCE

In the above 24 cases tabulated from the literature, 15 occurred in females and only 8 in males. (One case report from New Zealand did not specify the sex.) Surprisingly enough, in our series of 17 patients the very same ratio of 2 to 1 prevailed, with 12 subglottic hemangiomas in female infants and only 5 in males. So definite a similarity of findings would seem to be more than coincidental, yet a satisfactory explanation is as yet not apparent. In the very common cutaneous hemangiomas there is no such preponderance of females (MacCollum).

In our present series of 17 patients, 16 (or 94%) were diagnosed during the first 6 months of life, as the symptoms in most instances

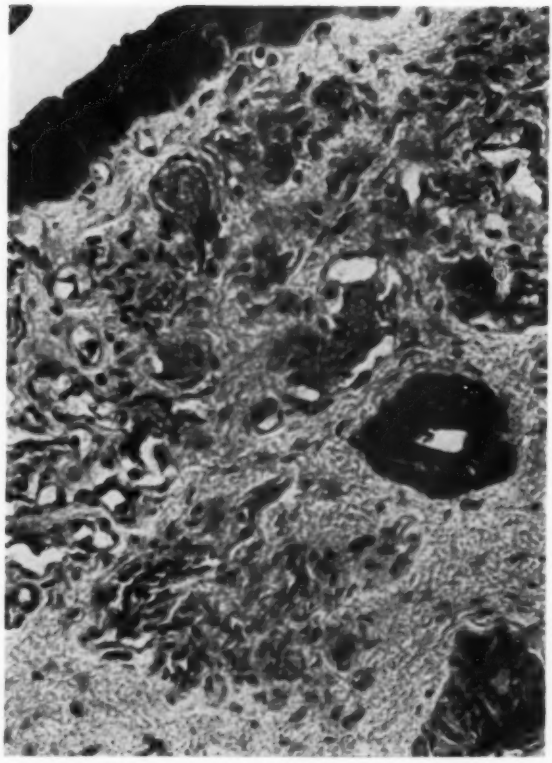

Fig. 1.—Biopsy Specimen (Hemangioendothelioma) (Case 4, Table II). Note intact pseudo-stratified laryngeal epithelium. Tumor shows large endothelial component, with relatively little vascular engorgement.

had been severe enough to warrant early investigation. They ranged from 2½ weeks to 6 months of age, except for one infant who showed milder symptoms and was not admitted until 2 years of age. In the series of 24 cases reported in the literature, the oldest was 11 months, and 88% were discovered either clinically or by autopsy during the first 6 months of life. Therefore, if hemangioma of the subglottic region is to give troublesome or serious symptoms, such difficulties develop almost always during the first 6 months of life. The condition can be regarded as probably congenital. If such lesions are not recognized and treated properly during this very early period, it seems

TABLE I

Case No.	Author	Age	Sex	Symptoms	Duration	Angiomas Elsewhere	Basis of Diagnosis	Treatment	Result
1	Phillips & Ruhl	9 mos.	M	Dyspnea, stridor and retractions	3 mos.	No	Autopsy	None	Asphyxia; death
2	New & Clark[5]	9 mos.	F	Dyspnea and stridor	6 mos.	No	Laryngoscopy	Radium—250 mg hr	Cure
3	New & Clark[5]	11 mos.	F	Dyspnea, cyanosis, retraction	5 wks.	Yes	History and angiomas elsewhere	Intubation and radium	Cure
4	Sweetser[6]	2 mos.	M	Dyspnea, cyanosis and retraction	7 wks.	No	Autopsy	Unsuccessful intubation	Submucosal hemorrhage of angioma due to intubation; asphyxia; death
5	Hofmann[7]	2 mos.	M	Dyspnea, stridor and retraction	Since birth	No	Laryngoscopy (confirmed by autopsy)	Tracheotomy and removal by laryngotracheal fissure	Postoperative pneumonia; death 1 month after operation
6	Hofmann[7]	2 mos.	M	Dyspnea, stridor and retraction	Since birth	Yes	Laryngoscopy (confirmed by autopsy)	X-ray therapy (400 r) followed by tracheotomy	Marked improvement for 16 days; death from pneumonia
7	Suehs & Herbut[8]	3½ mos.	M	Dyspnea, stridor and retraction	3 wks.	No	Autopsy	Tracheotomy	Massive atelectasis due to secretions; death
8	Ferguson[9]	2 mos.	F	Dyspnea, stridor and cough	1 wk.	Yes	Laryngoscopy and bronchoscopy	Tracheotomy and x-ray (600 r)	Cure
9	Kasabach & Donlan[10]	2½ mos.	F	Dyspnea and stridor	6 wks.	Yes	Laryngoscopy	Tracheotomy and x-ray (1300 r)	Cure
10	Kasabach & Donlan[10]	3 mos.	F	Dyspnea, stridor and retraction	3 days	No	Laryngoscopy and biopsy	Tracheotomy and x-ray (1280 r)	Cure
11	Sharp[11]	5 mos.	F	Dyspnea and stridor	4 mos.	Not stated	Bronchoscopy	Removal by laryngo-tracheal fissure	Cure
12	Dargeon & Daly[12]	3 mos.	M	Dyspnea, cyanosis and retraction	1 wk.	Yes	Autopsy	Tracheotomy	Asphyxia (due to mucous plug of tracheostomy); death

13	Rutherford & Sutherland[13]	4 mos.	Not stated	Dyspnea, stridor and retraction	2 mos.	Not stated	Path. exam of surgical specimen	Removal by laryngo-tracheal fissure	Cure
14	Ramsel[14]	3 mos.	F	Dyspnea, stridor and retraction	Since birth	No	Autopsy	Tracheotomy	Asphyxia (due to occluded tracheostomy); death
15	Doermann et al.[3]	1 mo.	F	Dyspnea, cyanosis and retraction	2 days	Yes	Autopsy	Tracheotomy	Asphyxia (secretions blocking tracheostomy); death
16	Baker & Pennington[2]	2½ mos.	M	Dyspnea, stridor	6 wks.	Yes	Bronchoscopy and x-ray	Tracheotomy and x-ray	Still tracheotomized*
17	Baker & Pennington[2]	1 mo.	F	Dyspnea, stridor		Yes	Laryngoscopy and bronchoscopy	Tracheotomy and x-ray	Cure
18	Holbrow[15]	3 mos.	F	Stridor	6 wks.	Yes	Laryngoscopy and biopsy	Tracheotomy and x-ray (250 r)	Cure
19	Holbrow[15]	?	F	Stridor	Since 6 wks. old	Yes	Laryngoscopy and biopsy	Only x-ray (450 r)	Cure
20	Campbell, Wigglesworth et al.[16]	3 mos.	F	Wheezing and stridor	2 mos.	No	Autopsy	No tracheotomy	Death
21	Campbell, Wigglesworth et al.[16]	7 wks.	M	Croup and wheezing	1 wk.	Yes	Autopsy	Tracheotomy	Death
22	Campbell, Wigglesworth et al.[16]	3 wks.	F	Wheezing and croup	4 days		Autopsy	Tracheotomy	Death
23	Campbell, Wigglesworth et al.[16]	3 mos.	F	Dyspnea	2 mos.	Yes	Laryngoscopy, no autopsy	Tracheotomy	Death
24	Campbell, Wigglesworth et al.[16]	3 mos.	F	Stridor, retractions	5 days	No	Branchoscopy and x-ray	Laryngofissure and x-ray (1800 r)	Cure
SUMMARY OF 24 CASE REPORTS:		21 out of 24 under 6 mos. of age	15 F 8 M 1 not stated			12 showed other angiomas	11 out of 12 autopsied; only 15 diagnosed during life (9 by autopsy)	15 tracheotomies 4 fissures 2 radium 9 x-ray	12 deaths 11 cures 1 still tracheotomized * 1 later decannulated

Fig. 2.—Autopsy specimen (hemangioma) (Case 6, Table II). Note larger, better filled endothelial spaces than in Figure 1, and less endothelial tissue component.

apparent that an extremely high mortality must be expected. As in other clinical conditions, the proper diagnosis will often not be made unless its possibility is seriously considered in the first place. Since so-called "congenital laryngeal stridor" is extremely common, the question naturally arises as to how many of the more severe cases die of respiratory obstruction from a subglottic hemangioma where the lesion is neither suspected antemortem, nor discovered postmortem.

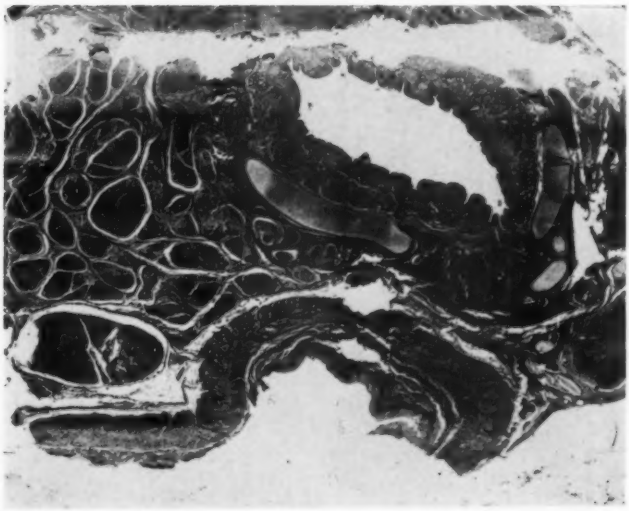

Fig. 3.—Cross section of neck (Case 6, Table II). Note tumor mass in laryngeal lumen, and also outside cartilages. Tumor surrounds esophagus.

PATHOLOGY

Although Mackenzie in 1864 is generally regarded as the first to report any type of hemangioma of the larynx, it was not until 1921 that Sweetser[6] differentiated between the infantile, subglottic lesion and the much more common cordal, or supraglottic, angioma of the adult. In 1944 George Ferguson[9] found that the cases in the literature comprised 90% adults with cordal lesions, and only 10% of the infantile subglottic type. The adult hemangioma of the larynx is ordinarily much easier to recognize, since it is usually cordal, for the most part reddish-blue in color, sharply demarcated, and often pedunculated, or at least projecting from the surface of the cord. On the other hand, the infantile type is characteristically subglottic, not so definitely colored, sessile and not so well delineated. A thicker layer of overlying normal mucosa may obscure the reddish color. Its surface is usually smooth and regular, and it does not appear nodular. This normal appearing mucosa over the subglottic swelling may lead an inexperienced observer away from the correct diagnosis. In our opinion, any localized, sessile bulging of the subglottic area, immediately beneath a cord, should be suspected as a possible hemangioma, even though the color may not be particularly typical of other hemangi-

TABLE II

Case No.	Name and Admission Date	Age	Sex	Symptoms	Duration	Angiomas Elsewhere	Basis of Diagnosis	Treatment		Result
								X-ray	Tracheotomy	
1	R.W. 4-17-51	6 wks.	M	Dyspnea, cyanotic attacks	Since birth	—	Laryngoscopy	300 r (once)	Outside hospital at 8 days	Cure (Decannulated at 1 yr.)
2	M.A. 6-17-51	2 mos.	F	Stridor and hoarseness; dyspnea	For 3 wks. For 24 hrs.	—	Laryngoscopy	300 r (over 3 days)	None	Cure
3	K.G. 3-12-53	4 mos.	F	Resp. distress; failure to gain	Since age 2 wks.	Yes	Laryngoscopy	500 r (over 2 days)	At 4 mos.	Cure (Decannulated at 2 yrs.)
4	R.M. 10-15-53	4 mos.	F	Progressive stridor	Since age 2 mos.	—	Laryngoscopy and biopsy*	1100 r* (100 daily for 11 days)	At 4 mos.	Cure (Decannulated at 14 mos.)
5	J.C. 3-31-54	8 wks.	M	Stridor, cyanotic attacks and retractions	Since age 3½ wks.	No	Laryngoscopy and bronchoscopy	400 r (over 2 days); 450 r (over 3 days 2 mos. later)	At 8 wks.	Cure (Decannulated at 21 mos.)
6	L.G. 11-15-55	2½ wks.	F	Progressive dyspnea and dysphagia	Since birth	Yes (Extensive of lip, chin, and face)	Laryngoscopy (tumor also supraglottic)	460 r (over 8 days)	At 3 wks.	Death (aspiration pneumonitis 2½ mos. after tracheotomy)
7	K.M. 11-29-55	7 wks.	F	Wheezing, dyspnea and cyanotic attacks	Since age 4½ wks.	Yes	Laryngoscopy	400 r (over 3 days)	Outside hospital at 5 wks.	Cure (Decannulated at 19 mos.)
8	J.W. 12-14-55	3 mos.	F	Cough, stridor and retractions	Since age 3 mos.	Yes	Laryngoscopy	450 r	Outside hospital at 2 mos.	Cure (Decannulated at 7 mos.)
9	S.C. 4-16-57	4½ mos.	M	Stridor	Since age 2½ mos.	No	Laryngoscopy	300 r (over 2 days)	None	Cure
10	K.S. 5-23-57	15 mos.	F	Stridor, retractions	Since birth	Yes (Extensive of face, head and neck)	Laryngoscopy	Radium therapy outside hospital	Outside hospital at 1 mo.	Cure (Decannulated at 2½ yrs.)

11	T.A. 12-27-57	2 yrs.	M	3 attacks "croup"; "cronic tracheitis"	Since birth	No	Laryngoscopy	200 r (over 2 days)	None	Cure
12	J.S. 2-3-58	4 mos.	F	Stridor, retractions	Since age 2½ mos.	No	Laryngoscopy	250 r (over 2 days)	None	Cure
13	L.S. 6-17-58	2 mos.	F	Stridor, retractions and wheezing	Since age 7 wks.	No	Laryngoscopy	200 r (once)	At 5½ mos.	Cure (Decannulated at 14 mos.)
14	E.C. 7-22-58	6 mos.	F	Stridor, "croup" attacks	Since age 2 mos.	Yes	Laryngoscopy	250 r (over 5 days)	None	Cure
15	K.P. 1-10-59	4 mos.	M	Stridor and croupy cough	Since age 3 mos.	Yes	Laryngoscopy	400 r (over 2 days)	At 4½ mos.	Cure (Decannulated at 13 mos.)
16	C.R. 7-28-59	3 mos.	F	Stridor, retractions and dysphagia	Since birth	Yes	Laryngoscopy	400 r (over 5 days)	At 3 mos.	Cure (Decannulated at 13 mos.)
17	C.H. 4-20-60	6 mos.	F	Stridor, "croup attacks"	Since age 2 mos.	No	Laryngoscopy	360 r (over 6 days)	None (Previously had temporary one at outside hospital at age 2 mos. for "croup"	Cure
SUMMARY OF RESULTS:		15 under 6 mos. 1 tracheotomized at 1 mo. but not seen till 15 mos.	12 F 5 M			8 angiomas elsewhere	All diagnosed endoscopically	All treated by x-ray	11 tracheotomies	16 cures (all decannulated) 1 death

* Tumor very solid; biopsy "hemangio-endothelioma"; therefore given larger radiation dosage.

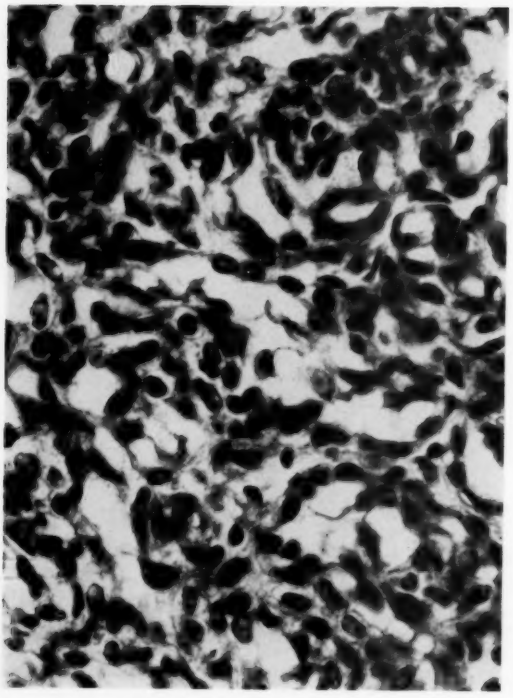

Fig. 4.—Higher power of subglottic hemangioma (Case 6, Table II).

omas. A larger endothelial component, relative to the vascular elements, produces a much more solid type of tumor, with more resistance to palpation, less compressibility, and more nearly the color of normal mucosa (Table II, Case 4).

Histologically, these lesions generally fall into the cavernous group of hemangioma, rather than into the capillary group (typical "strawberry marks"). In many cases, however, the capillary element may be very apparent. The tumor arises from the supporting structures of the larynx, and is therefore of mesodermal origin.

The overlying pseudo-stratified laryngeal epithelium is usually normal and appears intact, although it may be elevated or compressed by the growth. Relatively large endothelial-lined spaces vary in size,

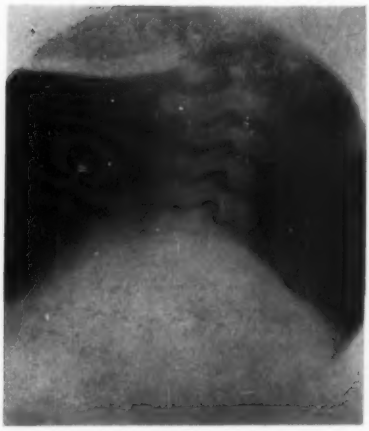

Fig. 5.—Lateral roentgenogram of neck. Note large subglottic mass posteriorly, with considerable encroachment of airway.

depending upon the amount of vascular engorgement, and this variation results in remissions and exacerbations of respiratory obstruction. These exacerbations may be misdiagnosed as "croup." Localized infection in the tumor, from a current respiratory infection, may play a part in the temporary increase in vascular congestion and engorgement, and thereby add to confusion in diagnosis. If these vascular spaces do not happen to be well filled at the time of the postmortem examination, the lesion may easily be missed by the pathologist, unless he has been trained to be alert to the condition. The endothelial cells of the tumor show a pale-staining cytoplasm, with a large ovoid nucleus. Connective tissue septa between the endothelial-lined spaces are usually thin. Mitotic figures are not common and the tumor is not malignant or invasive, even when apparently diagnosed as hemangio-endothelioma (as in Table II, Case 4).

CLINICAL COMMENT

No signs or symptoms were observed by us which could be considered pathognomonic of this condition. Approximately half of our patients had visible hemangiomas of the skin, but no such clues were present in the remainder. The signs which were observed were those usually associated with high respiratory tract obstruction of varying degrees of severity. Inspiratory stridor, the earliest and most con-

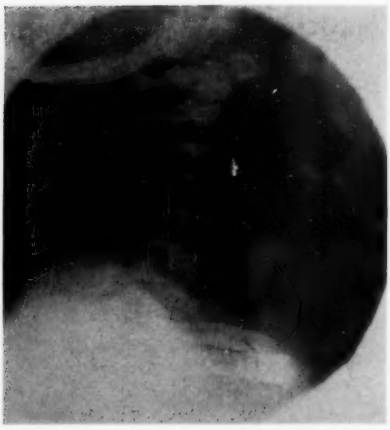

Fig. 6.—Lateral roentgenogram of neck. Note diffuse narrowing of subglottic region.

sistent symptom, appeared in all of our patients, usually early in the history, and persisted until relieved by tracheotomy, x-ray therapy, or a combination of the two. In two patients stridor was present at birth. One of these infants required a tracheotomy at eight days of age. In some instances, the signs of obstruction were progressive while in others these occurred in episodes separated by periods of remission, usually short. Several patients were thought to have recurring bouts of croup. The oldest patient in this series, age two, had three episodes which were considered to be croup, and was being treated for tracheobronchitis when first seen by one of us. Hoarseness was not a common symptom. The voice and cry were usually clear, but might be weak or muffled because of the limited respiratory exchange. Marked hoarseness was observed in one patient where the cords and supraglottic structures were involved by hemangioma, in addition to the subglottic lesion. The age levels in our series of patients were interesting in that 16 patients were six months of age or under when the diagnosis was made. One with milder symptoms was not seen until 24 months of age.

Stridor occurring in a young infant with a hemangioma of the skin should strongly suggest the possibility of another hemangioma in the subglottic area and requires a careful endoscopic examination in experienced hands. All of our patients were examined under general an-

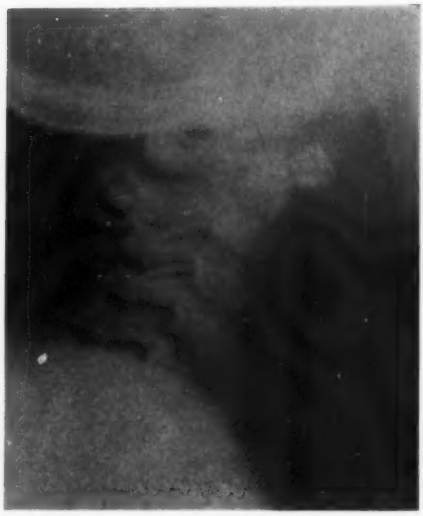

Fig. 7.—Lateral roentgenogram of neck. Note air in esophagus, outlining the subglottic obstruction.

esthesia since it has been our experience that lesions of this type, which are difficult to visualize at best, can better be discovered and properly evaluated in a tranquil patient than in one who is struggling and has to be controlled. The hemangioma usually appears directly below the cords and while more often unilateral, may involve both sides. These tumors vary from pink to blue in color, are easily compressible and project into the airway. In some instances the surface bleeds easily when touched. Biopsy was done in only one instance on a large, noncompressible, more solid, subglottic tumor mass, involving the right side of the larynx and occluding the airway (Fig. 1). In general, this maneuver is to be condemned since one might easily produce a severe or even fatal hemorrhage. The history of the condition, together with the location and endoscopic appearance of the obstructing tumor is, in our opinion, sufficient presumptive evidence of the nature of the lesion to warrant treatment without biopsy. So far as we know, there is no other tumor having similar appearance and characteristics which occurs in this location. The presence of skin hemangiomas would lend further support to the presumptive diagnosis. On occasions the lesion may be well outlined by an ordinary roentgenogram of the neck taken during inspiration when the airway is well

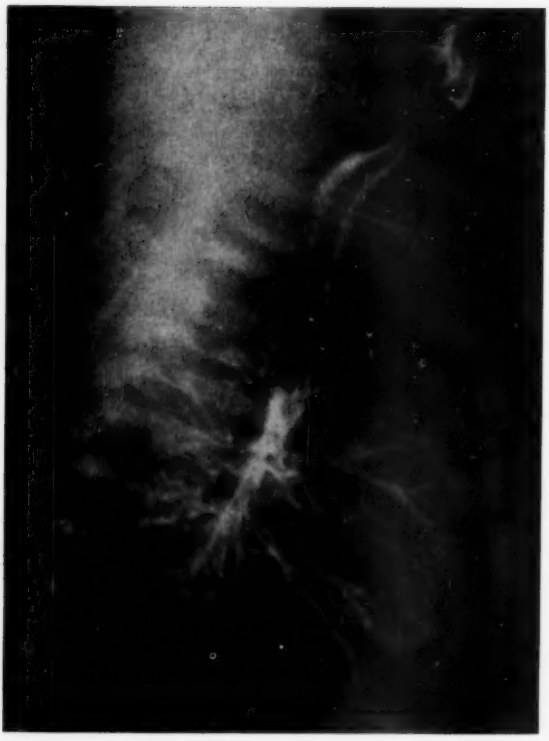

Fig. 8.—Lateral lipiodol tracheogram. Note prominent filling defect posteriorly in subglottic region.

filled. Figures 5, 6 and 7 illustrate the appearance of such a subglottic hemangioma. Tracheographic studies with radiopaque media on occasions will outline the tumor, but supply merely confirmatory evidence to the already performed, careful endoscopic examination (Fig. 8).

Where respiratory obstruction is marked or progressing, tracheotomy should be done when the diagnosis is made, since x-ray therapy is almost inevitably accompanied by some degree of swelling of the tumor and an increase in respiratory difficulty. Four of our patients had tracheotomy performed elsewhere because of laryngeal obstruction. In six instances tracheotomy was not required at all during the

course of the illness, and x-ray treatment was successfully accomplished without severe respiratory distress. In one instance it was necessary to perform a tracheotomy when obstruction resulted during the period while x-ray treatments were being given. Any patient undergoing x-ray treatment who has not had a tracheotomy should be hospitalized and placed under close observation during this period. It is our practice to put all of these patients in our high humidity rooms during this time whether or not a tracheotomy has been performed.

TREATMENT

In two of the earlier cases reported by New and Clark[5] (Cases 2 and 3, Table I), radium therapy had been employed, but since publication of their paper in 1919 no mention of such therapy has been encountered. In four other instances reported in the literature (Table II, Cases 4, 11, 13 and 17), the tumor was excised surgically through a laryngotracheal fissure. However, irradiation with x-rays is generally accepted today as the most effective treatment for hemangiomas in general, especially in regions not particularly amenable to surgical therapy. This modality succeeds in controlling rapid growth of the lesion, and leads to obliteration of the large vascular spaces with resultant permanent regression. It has retained the most widespread support. In the reports from the literature x-ray treatment was used in 9 of the 15 cases fortunate enough to be diagnosed antemortem. In 1945 Kasabach and Donlan[10] reported two infants treated by x-rays, but in these cases a total of 1200 r was used over somewhat less than a three week period. In 1956 Baker and Pennington[2] at Babies' Hospital in New York City advocated x-ray as the preferred method of treatment, and employed it in 100% of their 5 reported cases, which included supraglottic as well as subglottic lesions. In the formal discussion of their paper[2] we supported this method of therapy, and are still entirely in agreement, although since then we have reduced the total dosage considerably and have obtained as satisfactory results. They advocated 400 r given over a 9 day period, repeated at 3 monthly intervals until a total of 1200 had been administered. However, all of their cases presented very extensive cutaneous lesions of the head, face and neck, as well as the laryngeal lesions, and probably required a higher total dosage.

As stated above, biopsy of these hemangiomas seems unwise and unnecessary, unless the tumor is quite solid, or the diagnosis is truly uncertain. It definitely presents an increased hazard to the infant patient. Once the presumptive diagnosis has been established by

careful endoscopic examination under general anesthesia, either a tracheotomy is performed at once if the lesion is significantly obstructive, or the patient is started on his course of irradiation therapy. Throughout this period we believe he should carefully be observed in a high-humidity room in the hospital. Treatments are usually performed early in the morning, so that if edema is to become a problem, it should become apparent before the night hours. If no tracheotomy has been performed previously, it has been the policy of our Department of Radiology to give a smaller daily dose over a longer period of time in order to minimize any edematous reaction. Dr. G. J. D'Angio, Radiotherapist of the Children's Hospital Medical Center, to whom we are greatly indebted for such successful therapy, and for reviewing the present case reports, now advises employing a mere 40 r the first day, and gradually building up the dosage until 350 r has been given over a 4 to 6 day period. If the mass is not very large, and the airway good, the period of treatment is shortened to 2 to 3 days with a total of 250 to 350 r administered. When the infant has a tracheotomy, 250 to 350 r can safely be given at one time. In our entire series, the doses have varied from a total of 200 r to 500 r. In only one of the 17 infants (Case 5) who received 400 r over a 2 day period was a second course necessary, and two months later when it was apparent that the tumor had not responded quite satisfactorily, 450 r further was given over a three day period. Only in one other instance (Case 4) was it felt necessary to go above a total of 500 r, and this was in the case of the more solid tumor which biopsy had shown to be a hemangio-endothelioma (benign).

> The technical factors in use at our hospital at present are as follows: K.V. 200. M.A. 15. Filters added: 0.4 Tin, 0.25 Copper, 1.0 Aluminum. HVL is 2.7 mm of copper. TSD 50 cm. The portal is designed to include only the larynx, and the dose is delivered through opposing or oblique fields. A typical portal is only 2 to 4 cm.

Definite and ordinarily adequate response should be very apparent at least 6 to 8 weeks after treatment has been completed, as manifested by satisfactory regression of the tumor mass and improvement in the airway, when visualized by a followup endoscopic procedure. Except in the one instance as noted above (Case 5) all of the lesions regressed promptly after the initial treatment of a total of 500 r or less. Unfortunately, however, prompt decannulation was not always possible, and these patients present the same problem as other small infants who have undergone tracheotomy for different obstructive conditions such as acute laryngotracheitis. Within a matter of several

months, however, it was possible to decannulate every infant, and at present we have none who is wearing a tube or who has a fistula. In many instances the tubes were plugged almost constantly for weeks or months before it was deemed fully safe to remove them permanently, especially during the respiratory disease season of the winter months. In a few patients surgical closure of the fistula at a later date was necessary, especially if the tube had been worn for several months. In 11 of the group tracheotomies had been performed (4 before their first admission), but in 6 patients it was possible to make the diagnosis and carry out successful treatment with x-rays without resorting to tracheotomy. The end-result was excellent in all instances, except for the one infant who died unexpectedly of aspiration pneumonitis long after the treatment had been completed. Otherwise, she should have been recorded as a cure of the lesion.

SUMMARY

1. Subglottic hemangioma is an important, though frequently unsuspected, cause of respiratory obstruction or stridor early in infancy.

2. The lesion should be seriously considered if a localized subglottic bulge is seen, especially in the presence of a cutaneous hemangioma. Symptoms ordinarily begin before six months of age.

3. Females seem to outnumber males 2 : 1 both in the literature, and in our series as well.

4. The typical lesion of the infant is immediately subglottic, localized and sessile, and usually, but not always, red or bluish.

5. Carefully administered x-ray therapy, with or without tracheotomy, is the recommended method of treatment.

6. Twenty-four case histories from the literature with a 50 per cent mortality are briefly tabulated.

7. Seventeen patients from the Children's Hospital Medical Center in Boston are also reported, with satisfactory results in 16. All patients at present have been decannulated.

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LXXXI

LARYNGOSCOPY UNDER GENERAL ANESTHESIA

APNOEIC OXYGENATION TECHNIQUE

A REPORT OF OVER 100 CASES

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New York, N. Y.

Apnoeic oxygenation anesthesia is not new. It has been used in this country and abroad for several years, but it has been confined to bronchoscopy as far as the endoscopist was concerned.

At the American Academy of Ophthalmology and Otolaryngology meeting in 1959, we reported the use of this technique for laryngoscopy when we discussed Dr. Robert Priest's paper on general anesthesia for laryngoscopy.[1] Priest reported a large series of cases in which general anesthesia was given and maintained via the use of a Murphy endotracheal tube.

Our small series of apnoeic oxygenation anesthesia cases reported at that time seemed to offer such advantages that we have pursued its study and use with the co-operation of the Department of Anesthesiology at the Columbia Presbyterian Medical Center during the past year, and now report the results of over 100 cases done during that period.

The cases reported are those of both the attending staff and service cases of the resident staff. Likewise the anesthetics were given by both the attending and resident staff of the Department of Anesthesiology. In the latter department, approximately a dozen anesthesiologists participated.

The cases reported in this series were entirely among adults, whose ages ranged from 14 to 78 years. There were approximately three males to one female. The majority of examinations were for removing polypi, obtaining a biopsy, or for inspection of the larynx.

While there was some flexibility in the technique as to the medications given and the amounts used, the typical average technique was as follows:

Pre-operative medication with seconal 100 mg, followed by Demerol® 75 mg and atropine 0.5 mg.

In about half the cases the pharynx and larynx were sprayed with 2% Xylocaine.® We noted very little difference between those patients who did and those who did not receive the spray.

The patient was then allowed to breathe pure oxygen via the face mask for about ten minutes, with ranges of five minutes to twenty minutes. This fills the lung beds with approximately two litres of O_2 and, according to the studies of Frumin, Epstein, and Cohen,[2] permits oxygen saturation levels of 95 per cent to be maintained after three minutes of apnoea without additional oxygen insufflation.

When the patient is properly oxygenated, Pentothal® 250 mg is administered intravenously and once the corneal reflex is diminished, 100 mg of succinylcholine chloride is given. When relaxation is complete the laryngologist is advised to go ahead.

The laryngoscopy is carried out, the laryngoscope having been previously attached to a Lewy suspension apparatus.[3] In the majority of the cases the passing of the instrument, the removal of a growth, biopsy, or simple inspection were done in under two and a half minutes.

There were very few patients (about half a dozen) in whom the procedure was not completed within three to four minutes. In these the laryngologist removed his instrument, the anesthesiologist placed an airway in the hypopharynx, replaced the face mask, and repeated the oxygenation. After five minutes, together with whatever additional Pentothal and relaxant drug was found necessary, it was possible to repeat the procedure and complete the work.

The great majority of patients were fully recovered within ten minutes and were able to go directly to their quarters. A few, particularly those requiring additional medication, were sent to the recovery room and observed for longer periods. The patients in whom it was necessary to use greater amounts of relaxant drug were the only ones who occasionally complained of muscular aches lasting a day or two.

There were no complications among the first one hundred patients. Since then the method has been used in forty additional patients and among these there were two in whom the procedure was unsuccessful.

One was a 50-year old woman with bilateral polypoid vocal cords. It was impossible to visualize the larynx after two attempts. A third try was made and the patient developed extra systoles. The

procedure was discontinued. Under general anesthesia at a later date (given via a closed system and a tracheotomy tube), it still proved exceedingly difficult to expose the larynx. Eventually the vocal cords were stripped during two separate procedures with the anesthesia given via the tracheal stoma. Strangely enough, indirect mirror inspection had presented no difficulty.

The second patient was a 51-year old negro with hoarseness, whose vocal cords could not be visualized with indirect mirror inspection. He was admitted for direct laryngoscopy under apnoeic oxygenation anesthesia. Difficulty was encountered by the laryngologist due to a rather rigid jaw. This was followed by more relaxant drugs. On the third attempt, the patient became cyanotic after one minute with a pulse of 50, and blood pressure of 80/50. The anesthesiologist took over and introduced a pharyngeal airway. Forced ventilation with the bag was followed by passage of an endotracheal tube. After a short period the patient responded. There was an estimated cyanotic period of 3½ to 5 minutes. Ten hours later the patient developed myoclonic convulsions of the extremities which recurred intermittently for three days. He was transferred to the Neurological Institute and recovered under Dilantin® therapy. He remained alert and responsive during all of his myoclonic episodes, which could be initiated by touching him or jarring the edge of the bed. Repeated encephalograms were taken and he was discharged in one week with no residual sequela. He has refused any further inspection of his vocal cords.

COMMENT

This technique has now been carried out in a sufficient number of patients to feel assured that it is safe in the hands of a proficient and well-trained anesthesiologist.

The question has arisen regarding the use of this procedure in children and infants. The handicap here is that in these subjects the responses to medications are much more labile and involve greater risks. Fortunately the occasion for use of such a technique in this group is relatively rare.

It was thought that there might be added risks should one feel the need of using a cautery. After animal experimentation and inquiries from the Committee on Explosive Hazards, it was concluded that there was no added risk. In a few instances the small ball type cautery tip was used on the base of a removed hemangioma and granuloma.

This technique presents the advantages of a general anesthesia with the added benefits of no tubes being passed over a lesion and a completely unobstructed view of the larynx.

It is particularly recommended for procedures of short duration. It is, of course, of inestimable value for the apprehensive patient and those individuals with short thick muscular necks.

The only disadvantages would appear to be with those patients in whom one wished to study laryngeal function. The additional expense of a general anesthetic might be considered a handicap. The latter is not generally a problem with hospital insurance prevalent, and, if it were a problem, I am sure the relative ease of the procedure would make it well worth the added cost.

SUMMARY

We have reported the results of 140 cases of general anesthesia administered via the apnoeic oxygenation technique for laryngoscopies on adults. The lack of any serious complications seems to indicate that it can be regarded as a safe technique when administered by a qualified anesthesiologist.

It is particularly recommended for laryngoscopy of short duration. It affords the operator a completely relaxed patient plus an unobstructed view of the larynx.

156 East 37th St.

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LXXXII

ENDOSCOPIC SURGERY OF ZENKER'S DIVERTICULA

EXPERIENCE WITH THE DOHLMAN TECHNIQUE

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AND

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The pharyngo-esophageal diverticulum is a herniation of mucosa which begins in the posterior midline of the hypopharynx and extends through the weak point formed by the lowest oblique fibers and the circular fibers of the inferior constrictor muscle. These circular fibers constitute the cricopharyngeus muscle, which is the superior esophageal sphincter. It has long been regarded that the strong contraction and tone of the latter muscle, presenting a barrier to the swallowed bolus (possibly because of a disturbance of the swallowing mechanism), is an important etiologic factor in the formation of the protruding mucosal pouch. Zenker, in his classification, used the term pulsion diverticulum for this condition and, rightly or wrongly, considered diverticula of the thoracic esophagus to have origin in a process of fibrosis or contraction. The inco-ordination which develops between the constrictors of the pharynx and the cricopharyngeus muscle is probably a product of the process of aging and consequently, almost all cases of pulsion diverticulum are seen in patients over the age of 60.

In the early stages of development, the sac begins as a posterior mucosal bulge above the cricopharyngeus. Occasionally, a bit of food will lodge in the pouch and will have to be dislodged by forcible hacking and clearing the throat. Between these episodes, the patient may have no symptoms. As the sac grows larger and extends caudally into the superior mediastinum behind the esophagus, usually to the left of the midline, the opening into the sac becomes more dependent than the esophageal opening which is then compressed from posteriorly to form a slit-like opening and the esophagus itself, in this upper portion, is obstructed by the pressure of the contents of the sac. By this time, the symptoms will be quite severe and very distressing, not only to the patient but to the family or friends who share the

same table. Each swallow is an effort and is accompanied by the audible gurgling due to the regurgitation of the food and fluid in the sac. Laryngeal spilling and aspiration of the contents of the pouch cause fits of choking and gagging. Ultimately the patient develops a chronic bronchitis, repeated episodes of aspiration pneumonia, and occasionally a lung abscess.

The age of the patient and the debility which so often develops with long standing symptoms constitute a definite increased surgical risk. The use of the one-stage diverticulectomy in recent years was an advantage in the management of all cases of pulsion diverticulum and more particularly in these poor risk patients. The problems of the duration of the operation and the complications of fistula, pneumonia, vocal cord paralysis and recurrence must be considered in the older and more debilitated individuals. Medical management offers no symptomatic relief and the prognosis without surgery is therefore extremely unfavorable.

In 1958, Gösta Dohlman[1] described an endoscopic method of treating pulsion diverticula, whereby the cricopharyngeus muscle was cauterized and divided in the midline through a specially designed speculum (Fig. 1). In nearly 100 cases operated by this method, no deaths occurred and no severe complications were encountered. Recurrence rate is comparatively high but the ease of a re-operation endoscopically is in sharp contrast to the difficulty of a second external approach through the scar of a previous diverticulectomy.

The design of the endoscope allows easy insertion—an anterior lip passes into the esophagus and a posterior beak (Fig. 2) slides into the sac bringing the cricopharyngeus muscle clearly into view across the central portion of the visual field. The endoscope is inserted under general anesthesia with the airway maintained with an intratracheal tube. An alligator forceps (Figs. 3 and 4) with a sufficiently insulated shaft is passed through the endoscope and the dividing wall, the cricopharyngeus, is grasped firmly between the blades in the midline for a distance of 2.5 to 3 cms. The active pole of a cautery current is attached to a post on the forceps and the indifferent pole is attached to a similar post on the handle of the endoscope (Fig. 1). A strong coagulating current is applied until the tissue in the grasp is visibly cauterized. The forceps is then removed and a small spoon-like protecting insulator (Figs. 3 and 4) is passed into the sac just behind the dessicated tissue. Under direct vision, the cauterized portion of the pouch is then incised from anterior to posterior, using a cutting blade (Figs. 3 and 4) with a mixed cutting and coagulating

ANALYSIS OF CASES

			SYMPTOMS					FOLLOW-UP
Patient	*Sex*	*Age*	*Dysphagia*	*Regurg.*	*Cough*	*Duration*	*Date of Surgery*	
JP	M	64	X	X	XXX	20 yrs.	1-30-59	8 mos. later, no cough at present, 1½ yrs. P.O., sl. hesitation with coarse meats; 90% improvement.
CT	F	52	X	X	none	1 yr.	2-7-59	Recession of symptoms except some hesitation with coarse meats 1 mo.; 6 mos. P.O., no symptoms.
MP	F	59	X	X	X	10 yrs.	10-21-59	Nov. 13, 1959, hesitation with meats. March 1960, no symptoms.
EL	F	53	X	X	X	2 yrs.	11-14-59	Complete relief.
HT	M	70	none (Loss of Wt. - 12 LBS.)	X	none	1 yr.	11-21-59	Mild lump in throat after cold fluids.
VD	F	51	X	X	X	2 yrs.	2-3-60	No symptoms. Patient has rt. vocal cord paralysis following skull injury at age 24.
WH	M	66	X	X	X	2 yrs.	2-27-60	Complete recession of symptoms. Sac shows on x-ray to empty easily.
MM	F	79	X	X	X	16 yrs.	4-12-60	Eating all types of food. Notices some hesitation if he eats too rapidly.
WM	M	74	X	X	X	3 yrs.	4-20-60	Complete remission of symptoms.
RJ	M	72	X	X	X	1 yr.	10-19-60	Complete remission of symptoms.
DP	M	43	X	X	none	2 yrs.	5-11-61	No residual symptoms—too recent for adequate follow-up.

current. Pressing firmly against the protective shield, this incision accomplishes complete division of the cricopharyngeus. Bleeding at the cut ends of the tissue is minimal and is easily controlled by a pad of gelfoam which may be placed in the incision to complete the operation.

The patient is maintained on intravenous fluids for 48 hours and if no residual discomfort is noted at that time, clear liquids are

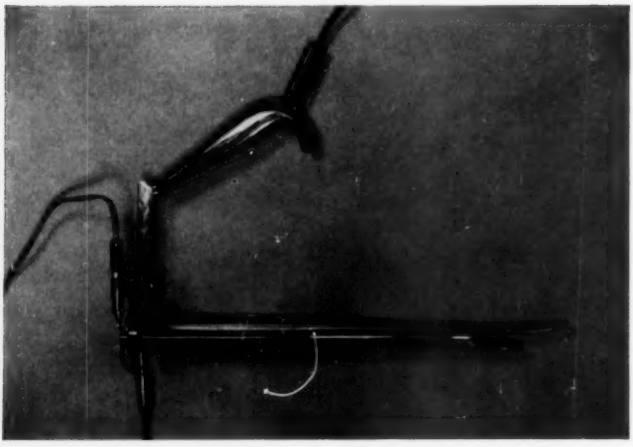

Fig. 1.—Dohlman endoscope with slotted tip used in exposure and sectioning of cricopharyngeus muscle and diverticulo-esophageal wall.

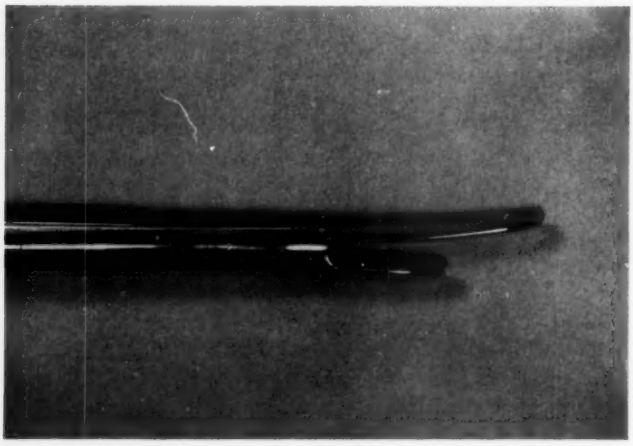

Fig. 2.—Enlarged view of endoscope tip with horizontal slit between the anterior lip and the posterior beak.

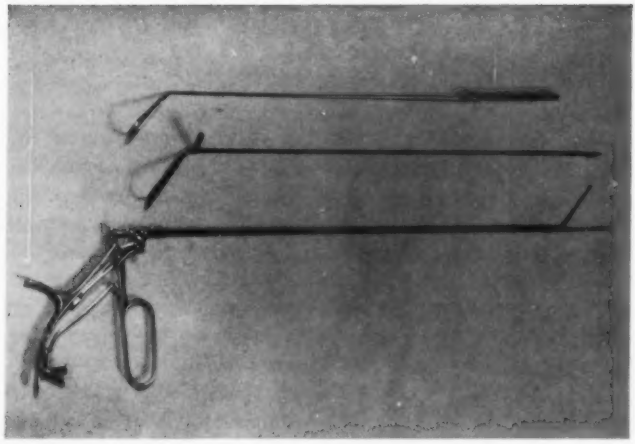

Fig. 3.—A) insulated protective bar; B) insulated scalpel; C) insulated alligator forceps.

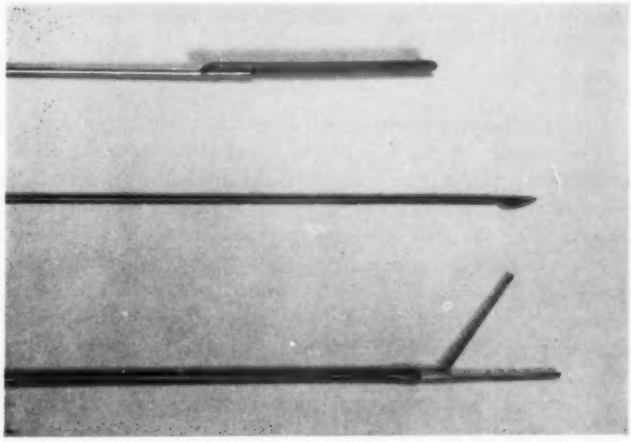

Fig. 4.—Enlarged view of tips of instruments used in endoscopic division of cricopharyngeus muscle.

allowed by mouth. In 24 hours, the diet is increased to include mechanically soft foods for another 48 hours after which time a modified soft diet is permitted as tolerated. The patient is usually ready to leave the hospital on the fifth postoperative day swallowing easily and without discomfort. A general diet is permitted two weeks after the operation.

Since January 1959, the authors have performed eleven diverticulotomies using the Dohlman technique. This series was comprised of six males and five females—the majority being over 60 years of age. The youngest was a 43 year old male and the oldest, a 79 year old female. All had complained of dysphagia and regurgitation and all but two had an associated cough—one patient (M.P.) had a lung abscess which cleared on conservative treatment. The minimum duration of symptoms was one year and the maximum was 20 years.

Following the operation all noted cessation of coughing and relief from regurgitation. Six patients had no further dysphagia, one had a sensation of a lump in the throat after ice cold drinks and one had some hesitation during the swallowing of coarse meats which disappeared after six months. Two patients continued to have slight hesitation with coarse foods and one noted a hesitation when eating too rapidly. One patient in this series has been too recently operated to correctly assess the final postoperative result.

COMMENT

Although the procedure of splitting the cricopharyngeus muscle by the endoscopic approach is not a recent discovery, the technique of the Dohlman method appears very definitely to produce satisfactory results with safety. The important feature in this operation would seem to be the complete section of the muscle while the cautery acts as a seal to prevent hypopharyngeal and upper esophageal leakage into the mediastinum. It is surprising that often the size of the sac postoperatively is little changed and the sac may be seen on fluoroscopic studies to fill momentarily much as it did before surgery. But the physiologic elevation of the pouch on swallowing quickly empties the contents into the esophagus when the constricting band of muscle no longer prevents this maneuver. The patient swallows without difficulty and without regurgitation; and since the sac contains no residue of food, fluid or secretions, laryngeal overflow is absent and the pulmonary complications improve or disappear completely. The endoscopic method of treating a pulsion diverticulum has proven to be of exceptional value in the elderly poor risk patients. The short

duration of the procedure and the ease with which it is accomplished minimizes the postoperative complications and reduces the operative hazards.

SUMMARY

Hypopharyngeal pulsion diverticula can be successfully managed by incision of the cricopharyngeus muscle endoscopically. The Dohlman method of performing this operation permits easy exposure of the constricting muscular band through a specially designed endoscope. A cauterizing forceps prepares the area to be incised between the sac and the esophagus. The cutting blade separates the two sides of the partitioning wall and provides a free channel from the sac into the esophagus. Eleven patients with pulsion diverticulum treated by the endoscopic approach are reported in this series as a preliminary report. No postoperative complications have been observed and all have had satisfactory relief of symptoms. Subsequent fluoroscopic studies have shown that the sac remains essentially unchanged in size but empties freely into the esophagus. No residue can be seen in the sac after a swallow of light barium, and with heavy barium the sac is emptied after one or two subsequent swallows. The short duration of the operation and the reduced period of hospitalization are of special benefit in the management of elderly patients and those who are considered poor surgical risks.

700 N. Michigan Ave.

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LXXXIII

LOWER ESOPHAGEAL DISEASE IN INFANTS AND CHILDREN

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We ordinarily think of the lower end of the esophagus as that part of the esophagus contained in the lower thorax which passes through the hiatus of the diaphragm joining the stomach a centimeter or so below the hiatus. On the other hand we must remember that the true lower end of the esophagus may be quite high in the thorax as in congenitally short esophagus, and also after surgical repair of certain congenital esophageal anomalies such as atresia of the esophagus.

The esophagus may be described as a two layered muscular tube extending from the pharyngeal musculature, namely the cricopharyngeus, to the muscular wall of the stomach. The level of the proximal end is at the cricoid cartilage and the distal end is demarcated by the reflection of peritoneum from the stomach to the inferior surface of the diaphragm. This tube is lined by epithelium and to quote Hayward,[1] "The esophageal lining should be described as having mainly stratified squamous epithelium with glands in the submucosa, but partly columnar epithelium with glands in the mucosa and variable small islands near the upper end and around the whole circumference of the lower one or two centimeters. The stomach should be described as being lined by two sorts of epithelium, fundal and pyloric, except a very small area around the esophageal opening where the esophageal junctional epithelium protrudes into it."

To amplify the above statement, Hayward has described the epithelium between the squamous epithelium of the esophagus and the gastric epithelium as being columnar. This columnar epithelium has simple tubular glands which produce mucus only and not digestive juices. He further described this area of mucosa to be very mobile resulting in changes in appearance with esophageal and gastric movement. In the past this columnar epithelium has been considered by

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Barrett[2] and others as gastric epithelium. Hayward has coined the term "junctional epithelium." To the essayist this seems to be a very suitable term.

Although the word "cardia" has been used quite freely to describe the lower end of the esophagus, the exact location of the cardia is often not clear. Hayward defines the cardia as "the sphincteric lower part of the esophagus between the phreno-esophageal ligament and the gastro-esophageal junction."

Diseases of the lower end of the esophagus may be described under three headings, namely: 1) congenital; 2) acquired diseases secondary to congenital defects; and 3) acquired diseases.

CONGENITAL ATRESIA OF THE ESOPHAGUS

The commonest congenital anomaly of the esophagus is atresia with or without a trachea-esophageal fistula. Although the atresia may be near the lower end of the esophagus, esophagoscopy does not usually play a part in the diagnosis and certainly not in the treatment at this stage.

CONGENITAL STENOSIS

Congenital stenosis of the esophagus is relatively uncommon and may involve any part of the esophagus including the lower end (Fig. 1). Holinger[3] has described two distinct types of esophageal stenosis. One type is that in which there is a tight fibrous stricture and the other the failure of epithelization of a segment of the esophagus. The degree of symptomatology will depend on the severity of the stricture. These patients are often difficult to feed and are slow to take their feedings but severe dysphagia does not usually take place until the child begins a semi-solid or solid diet. Diagnosis may be made by roentgenograms which show an abrupt narrowing of the esophageal lumen and often a certain amount of dilatation above the stenosis. Esophagoscopy reveals a marked narrowing of the esophageal lumen at the site of the stenosis. The esophageal mucosa above the stenosis is fairly normal in appearance unless there has been an esophagitis due to retained food.

It has been our experience that this type of stenosis responds very readily to dilatation either by direct dilatation from above or by retrograde dilatation in the very marked strictures. In reviewing the case records at our hospital, we found many cases that were diag-

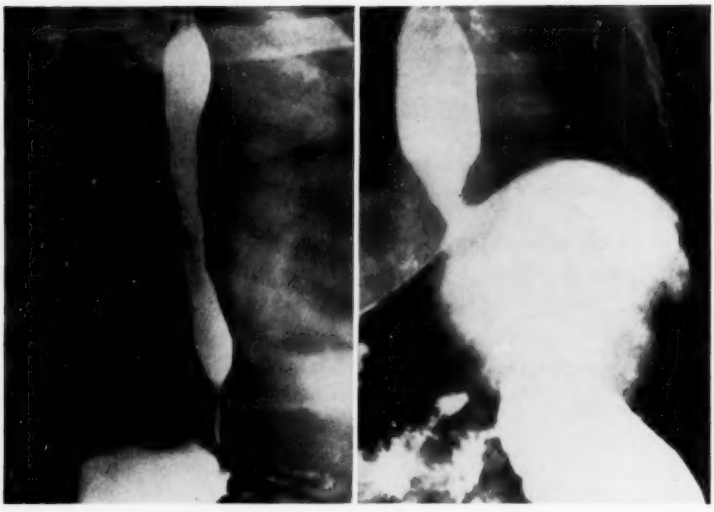

Fig. 1.—Congenital stenosis of the lower esophagus.
Fig. 2.—Chalasia.

nosed at one time as congenital stenosis of the esophagus were actually strictures secondary to esophagitis associated with a hiatal hernia.

CONGENITAL WEBS

Congenital webs of the esophagus also may occur in any part of the esophagus and may be multiple. The webs present the same symptomatology as a stenosis and the endoscopic appearance is much the same as the stenosis. Esophagograms however will show a definite distinction between the two. Fortunately webs respond particularly well to simple dilatation.

ACHALASIA

In our experience achalasia, or cardiospasm, is relatively uncommon in children. Moersch[4] and Holinger[3] have reported cases of cardiospasm in newborn infants although the youngest patient we have seen has been four years of age. The etiology of achalasia is still unknown. It is considered to be due to a neuromuscular incoordination of the cardia and this results in dilatation and hypertrophy

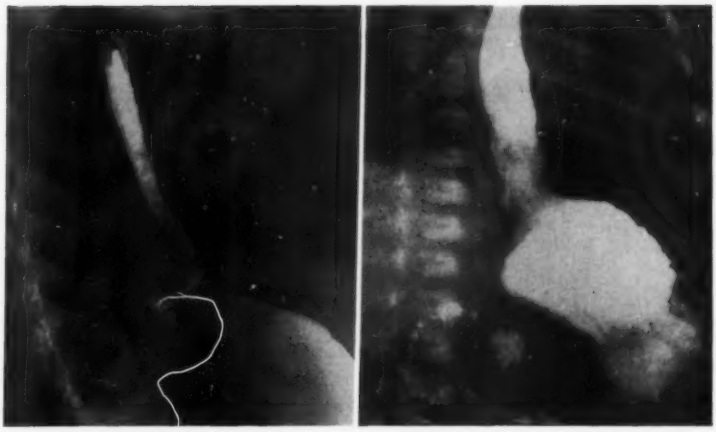

Fig. 3.—Diverticulum of the lower esophagus. Patient has a stricture secondary to a hiatal hernia plus a foreign body (coin).

Fig. 4.—Hiatal hernia—patient had a severe peri-esophagitis with a deep ulcer at the age of six weeks.

in the walls of the esophagus. The obstruction seems to be due to muscular spasm at the cardia although in some instances it appears to be a fibrous stricture involving the cardia in association with muscular spasm. This problem may be controlled quite satisfactorily with direct dilatation with the esophagoscope or with Hurst bougies. If simple measures fail the hydrostatic bag may be used, or gastrostomy carried out and retrograde dilatations performed. The Heller operation may be necessary in severe problems. Investigation of esophageal motility by Olsen and Creamer,[5] Siegel and Hendrix,[6] and others has added much to our knowledge, not only in the normal esophagus, but particularly in relation to achalasia.

Cineradiography is also an important adjunct in providing information about esophageal pathology. Creamer[7] has made simultaneous pressure measurements and cineradiography with interesting results.

CHALASIA

Chalasia is a congenital condition which is opposite in character to that of achalasia (Fig. 2). The cardia remains widely patent so that there may be continual reflux from the stomach into the esopha-

gus and thus result in regurgitation or vomiting with bouts of choking. These patients have no difficulty in feeding but only difficulty in retaining their feeding in the stomach. In most instances this problem may be managed conservatively in the same manner as one would treat a sliding hiatal hernia. In the severe problems surgical correction may be necessary.

DIVERTICULA

Diverticula of the esophagus are usually incidental findings and ordinarily do not give rise to symptoms (Fig. 3). Ectopic gastric mucosa may be present in these diverticula giving rise to ulceration and bleeding.

ESOPHAGEAL HIATAL HERNIA

This is a condition in which there is a displacement of the distal esophagus and a part of the stomach into the thorax through the hiatus of the diaphragm. There are primarily three groups of esophageal hiatal hernia, namely: 1) hiatal or sliding hernia; 2) para-esophageal or rolling hiatal hernia; 3) congenitally short esophagus with thoracic stomach, or simpy brachyesophagus. This condition is a very controversial one and there is such a great variation of opinion regarding the etiology and treatment that one must depend on one's own observation and experience in assessing these conditions. There is not time in this paper to consider the various theories of etiology. The most important element in the pathology of hiatus hernia is the physiological failure of the diaphragmatic pinch-cock resulting in reflux of acid gastric peptic secretion into the esophagus (Fig. 4). Whether the primary failure of the pinch-cock is due to a congenital deficiency of the right crus in the posterior margin of the hiatus or to a defect of the phreno-esophageal ligament, is uncertain; Allison[8] is in favor of the former view and Harrington[9] and Hayward[10] the latter. A hernial sac is always present when the recessed peritoneal cavity projects upward through the hiatus in front of the stomach. The symptoms of hiatus hernia are largely those of its complications.

The occurrence of herniation in early infancy supports the view that hiatus hernia should be regarded as congenital in origin, based upon a developmental abnormality of the diaphragm.

In our experience there appear to be two distinct types of the problem as seen by esophagoscopy. In the majority of our cases the esophagogastric junction has been high and the hiatus quite patent

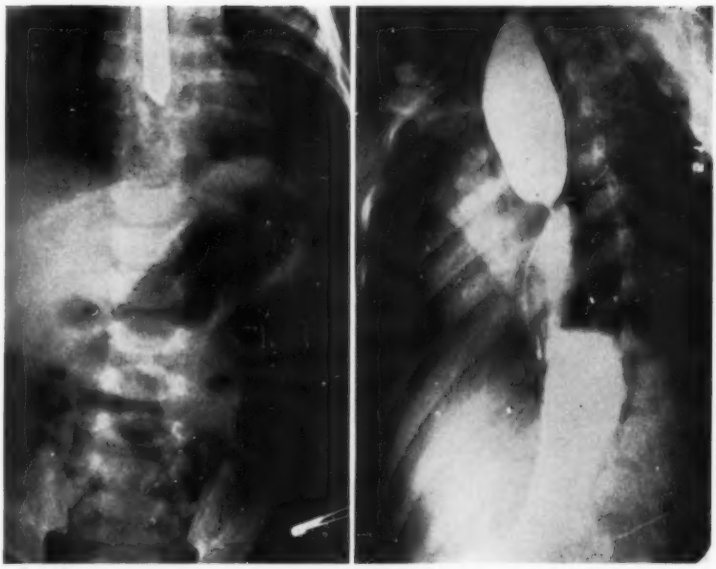

Fig. 5.—Manner of locating esophago-gastric junction in a hiatal hernia.
Fig. 6.—Stricture secondary to what may be a congenitally short esophagus.

with no obstruction to the esophagoscope in its passage into the abdominal stomach. In a smaller number of patients the esophago-gastric junction is high and the hiatus itself offers considerable resistance to the passage of the esophagoscope through it. In the former cases there seem to be less reaction in the esophagus, the main symptom is vomiting without hematemesis and there is less esophagitis apparent on endoscopy. In the latter type we find that the esophagus has usually a much more severe reaction and in these cases we seem to have a greater proportion of strictures. The chief signs and symptoms of hiatal hernia are vomiting and regurgitation which in turn may result in bouts of choking and severe respiratory distress, repeated pneumonia, or repeated bouts of bronchitis. The vomiting and dysphagia may result in dystrophy. Hematemesis, melena and severe anemia may result from severe esophagitis and bleeding from the esophageal mucosa. In 50% of the patients observed, symptoms dated from birth, and another 26% had symptoms beginning under one year. There is very definite danger of asphyxiation due to aspiration of vomitus.

Diagnosis of esophageal hiatal hernia is made by roentgenography and esophagoscopy. Putney[11] has shown that roentgenography alone cannot be depended upon to establish the diagnosis and we believe that the diagnosis by roentgenography is even more difficult in children and infants than in adults.

Our method of determining the diagnosis of hiatal hernia by esophagoscopy is to carry out the endoscopy under general anesthesia via the endotracheal route and using the fluoroscopic table. The esophagogastric junction may be identified by the change in the smooth folds of the esophagus to the typical gastric rugae. The tip of the esophagoscope is placed at the esophagogastric junction and its position relative to the dome of the diaphragm as determined by fluoroscopy (Fig. 5). Because of the problem of reflux of gastric secretion, we use an aspirating esophagoscope to facilitate identification of the esophagogastric junction as well as to visualize changes in the esophageal mucosa as a result of gastric secretion.

PARA-ESOPHAGEAL OR ROLLING HIATAL HERNIA

This congenital defect in the esophagus can be diagnosed only by roentgenography—esophagoscopy plays no part in the diagnosis or treatment.

CONGENITALLY SHORT ESOPHAGUS

Congenitally short esophagus or brachyesophagus is probably quite uncommon. It is most difficult to distinguish between this and a sliding hiatal hernia with secondary changes by esophagoscopy or roentgenograph. There is probably no sure way of distinguishing between the two except by thoracotomy or at postmortem.[12] Clerf and Manges[13] have reported that the essential points in the roentgen ray diagnosis of congenital shortening of the esophagus are, first, a portion of the cardiac end of the stomach must be shown to stay above the level of the diaphragm; second, the esophagus must be shown to be too short to reach as low as the level of the diaphragm (Fig. 6). However these same features may be found in the sliding type of hiatal hernia where there have been secondary changes in the esophagus.

DISEASES OF THE ESOPHAGUS ACQUIRED SECONDARILY TO CONGENITAL DEFECTS

Although sliding hiatal hernia has been described as a congenital defect we feel that the secondary changes resulting from this condi-

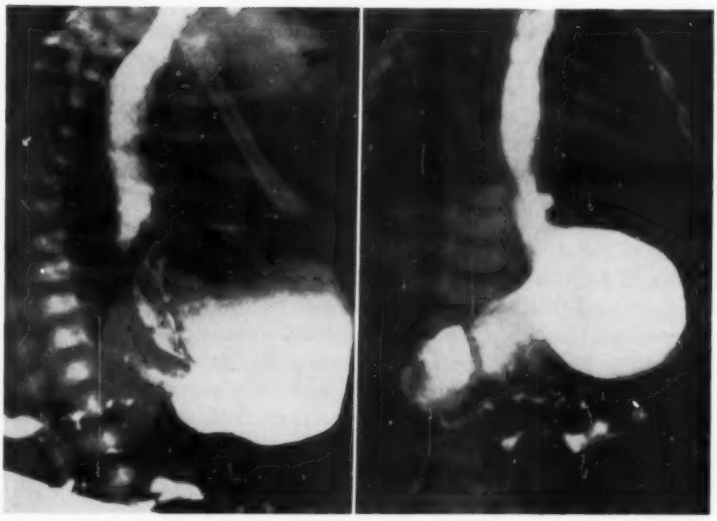

Fig. 7.—Severe esophagitis with hematemesis secondary to hiatal hernia at age of nine days.

Fig. 8.—Hiatal hernia with "Barrett's Ulcer," age five weeks.

tion should be considered as being acquired. According to Hayward,[1] dysphagia from sliding hiatal hernia is due to inflammatory hyperemia and edema in the esophagus, to esophageal muscular inco-ordination or spasms, or to laying down circumferentially of dense contracted fibrous tissue in the mucosa, submucosa or all the layers of the esophageal wall. He feels the strictures do not occur at the esophagogastric junction but rather at the point where the squamous epithelium ends in the distal esophagus. Due to a process of metaplasia of the squamous epithelium secondary to esophagitis, the stricture may then occur a considerable distance proximally from the gastric mucosa. In small children we have found the strictures very close to the esophagogastric junction, probably because the metaplastic changes seen in adults occur over a long period of time, whereas in children the esophagitis may occur very early and strictures may form very early. Endoscopically, changes in the esophagus may vary from a mild inflammatory reaction in the immediate area of the esophagogastric junction to inflammation and ulceration of nearly the whole length of the esophagus. These reactions may occur amazingly early in life with rather marked stricture formation at the age of four weeks,

extensive ulceration at nine days (Fig. 7) and a rather deep ulcer at five weeks of age (Fig. 8). Severe respiratory distress was encountered in a child aged two days necessitating tracheotomy, and only when the hiatal hernia was repaired at the age of three months could the tracheotomy tube be removed because of frequent vomiting and aspiration of vomitus prior to the hernia repair. All infants with an esophageal hiatal hernia are in danger of massive aspiration of gastric contents and thus asphyxiation.

It is the function of the esophagoscopist to determine the diagnosis of hiatal hernia but also to assess the state of the esophagus in order to provide a guide for future management. When a stricture is present it is dilated as a stricture from other causes but in most instances dilatation alone will not solve the problem. It is better that the hiatal hernia be repaired and then the stricture dilated until a satisfactory lumen is present. It has been our experience that very little dilatation is required after the esophagitis has been eliminated by hernia repair.

In a series of one hundred and one cases of esophageal hiatal hernia under our observation, the symptoms and esophageal changes were sufficiently severe to warrant surgical repair in 25.[21]

STRICTURES SECONDARY TO SURGICAL REPAIR OF THE ESOPHAGUS

In most instances wherein atresia of the esophagus has been surgically corrected, the site of the stenosis is high in the esophagus. In some instances the stomach may be brought up into the chest in order to do a direct anastomosis to the upper segment of the esophagus. In spite of the fact that one would expect a reflux esophagitis in such cases, we have not found this to be a problem.

While attempting to anastomose the two segments of the esophagus in an esophageal atresia with tracheo-esophageal fistula, it may be necessary to free the stomach and bring it partially into the thorax in order to avoid undue tension at the suture line.[14] This creates in effect an hiatal hernia which in turn will cause the patient to suffer the problems of hiatus hernia. Stricture occurred in such a patient at the age of four weeks (Fig. 10). This hernia was repaired. Hiatal hernia repair has been necessary in several such patients including patients with tracheo-esophageal fistula without esophageal atresia.[15]

One of the most difficult problems we have encountered is that in which a colon transplant has been used to bridge the gap between

the small upper segment of the esophagus and the stomach in a severe esophageal atresia. The stricture tends to form not only at the proximal anastomosis but also at the anastomosis between the colon and stomach. Retrograde dilatation is the only safe way of treating these strictures but getting the string through the transplanted colon is a most tedious procedure. To find the distal opening by retrograde esophagoscopy is almost impossible and great care must be taken in doing direct esophagoscopy because of the fragility and redundancy of the colon transplant.

ESOPHAGEAL VARICES

In children, esophageal varices are most often secondary to extrahepatic portal hypertension. The serious aspect of the disease is severe hemorrhage from the esophageal varices and the youngest patient with whom we had to deal was a twenty-three month old girl.[16] The most satisfactory method of correcting the portal hypertension is to carry out a splenorenal or portacaval shunt. It is felt by our surgical staff that the results in either operation are not good when performed before the child is ten years of age. We have been able to control the bleeding in approximately 70% of the patients with extrahepatic portal hypertension by the injection of sclerosing agents into the varices. Injection of esophegeal varices has not been carried out as a definitive treatment but rather to maintain the patient in relatively good health until there is more likelihood of success by a shunt operation. Recently we esophagoscoped the first patient in our series six years after he was first injected. Shunting operations have been tried subsequently but were not successful. However the boy has had virtually no bleeding since the first injection and has had no bleeding whatsoever for four years and has been living a normal healthy life. Recent esophagoscopy showed only remnants of the sclerosed varices.

ACQUIRED DISEASES OF THE ESOPHAGUS

Tumors. Tumors of the esophagus in infants and children are extremely rare. We have seen only one neoplasm at the lower end of the esophagus which proved on biopsy to be a reticulum cell sarcoma (Fig. 9). This fifteen year old boy was esophagoscoped because of dysphagia and a large tumorous mass was found at the lower esophagus extending into the stomach. It had the appearance of a lipoma but biopsy revealed the diagnosis. Resection of the lower end of the esophagus and a subtotal gastrectomy were carried out and this was followed by a course of irradiation. This patient is alive and well and has had no recurrence after eight years.

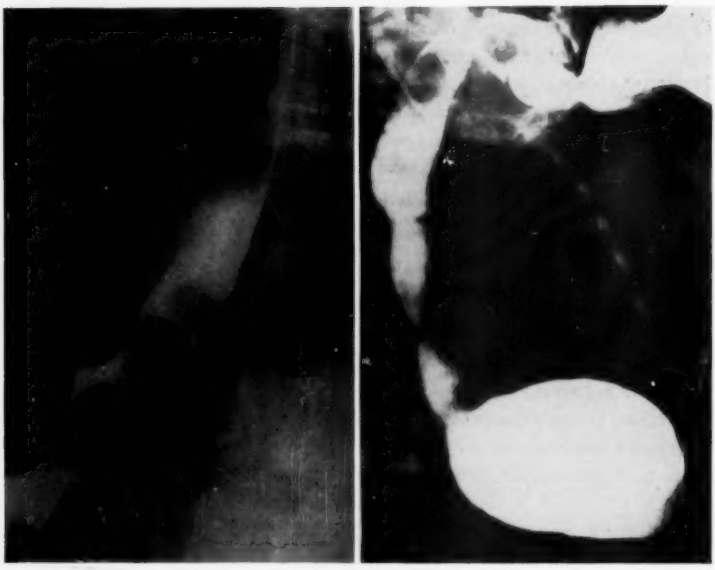

Fig. 9.—Reticulum cell sarcoma.

Fig. 10.—A repaired atresia of the esophagus with tracheo-esophageal fistula with a hiatus hernia and secondary stricture.

Foreign Bodies. Foreign bodies in the esophagus most commonly lodge in the upper third except for occasional ones with points or sharp corners. Whenever a foreign body, particularly a smooth one, lodges in the lower esophagus, a lesion of the esophagus distal to the foreign body should be suspected and investigated.

Peptic Esophagitis. Peptic esophagitis due to reflux may occur in a severely ill comatose patient and we believe this is more likely to occur if a feeding tube has been left in the esophagus for a long period of time. The feeding tube will tend to prevent the normal pinch-cock action at the esophagogastric junction and thus permit the reflux of gastric secretions into the esophagus.

In children acute primary esophagitis is not commonly diagnosed. No doubt in many instances of severe vomiting a varying degree of esophagitis does occur which, however, has not been severe enough to warrant esophagoscopic investigation. We have seen one three

year old boy with Steven-Johnson's syndrome (erythema multiforme) develop an esophagitis in the lower esophagus which subsequently went on to a rather severe stricture formation. Gastrostomy and retrograde dilatations were necessary for a few weeks but when the systemic disease was controlled and with the cessation of esophagitis the stricture dilated easily and has not needed attention for four years. It would seem possible that in this case the esophagus may have been involved as a part of the Steven-Johnson's syndrome.

Perforations. Spontaneous rupture of the esophagus in children is very unusual although one patient developed a perforation of the lower esophagus into the mediastinum during a bout of violent vomiting associated with the endobronchial rupture of a previously untreated lung abscess. Although the boy was acutely ill for several days he responded to treatment and the perforation closed spontaneously. However a stricture developed at the site of the perforation which subsequently required treatment.

Instrumental perforation of the lower end of the esophagus is most likely to occur from blind bouginage in the treatment of strictures. Since the esophagus is often dilated above a stricture, a bougie or a tip of the esophagoscope may enter a pouch and it takes very little effort to perforate the esophageal wall (Figs. 11 and 12). The wall at this point may be thinner than otherwise because of the stretching of the muscular layers and possibly this makes a perforation more likely to occur. Wherever possible immediate thoracotomy and closure of the perforation should be attempted.[17] If immediate closure of a perforation is not feasible, and an esophago-pleural fistula is present, closed drainage of the chest is the treatment indicated.

Corrosive Strictures. In the patients treated at the Hospital for Sick Children corrosive strictures due to lye and other caustics are more common in the upper half of the esophagus. Nevertheless strictures do occur at the lower end of the esophagus either with or without upper esophageal involvement.

Treatment of the acute phase of corrosive esophagitis is a controversial one and time does not permit us to go into detail concerning this. However we prefer not to carry out instrumentation in the obvious esophageal burns for a week to ten days after the ingestion of the corrosive agent and only when the dysphagia is no longer present. We feel at this time we can evaluate the esophagus quite safely and then decide the future course of treatment that is likely

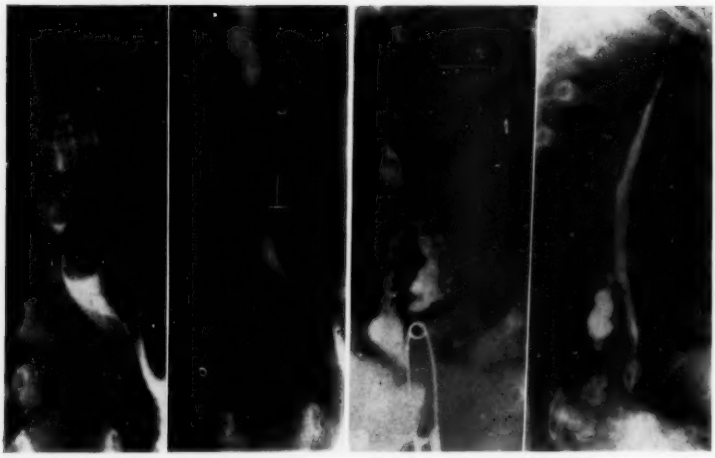

Fig. 11.—Corrosive stricture with a diverticulum.
Fig. 12.—After instrumentation.

to be necessary. We believe that the endoesophageal skin graft as previously described by us offers the best solution to many of the annular types of stricture.[18] Strictures of the lower end of the esophagus are most amenable to this procedure since at the lower end one does not have to worry about the problem of compression of the trachea by the mould over which the skin is placed in doing the graft. When any stricture of the esophagus, whether it be acquired from ingestion of corrosives, surgical anastomosis of the esophagus, or stricture secondary to a hiatal hernia, is not responding satisfactorily to dilatations, then a reflux esophagitis must be suspected and investigated. Recently a boy, who had received dilatations for several years to a stricture resulting from ingestion of lye, was referred to us for esophagoscopic evaluation. We found a moderately severe stricture at the lower end of the esophagus with signs of esophagitis proximal to the stricture. The stricture dilated up fairly readily and when a small esophagoscope was passed beyond the stricture we felt the boy had a hiatus hernia as well. We suspected the lack of response of the stricture to treatment was due, in part at least, to reflux secondary to the hiatal hernia which itself may have been caused by shortening secondary to fibrosis of the esophagus from the corrosive injury years before. The boy then had a hiatal hernia repair but we have not yet re-assessed the esophageal status.

The esophagograms in this patient reveal an important point in evaluating such strictures in that when the stricture is quite small the esophagus below the stricture will not fill. Thus the stricture appears much longer than it actually is. Esophagograms taken after the dilatation in this case provide a better indication of the actual length of the stricture.

In the light of great advances made in esophageal surgery in recent years there is a strong tendency among many thoracic surgeons to resect the strictures and either do an anastomosis of the normal parts of the esophagus, or to perform some type of surgery such as colon transplant to provide continuity from the normal esophagus to the stomach. However Holinger[19] and his colleagues have pointed out that dilatation of esophageal strictures should be continued until it becomes apparent that a functional esophagus cannot be obtained by conservative measures. With this statement I heartily agree, for although repeated bouginage may be a trial to the patient, there is no guarantee that the more major surgical procedure is going to eliminate a problem of swallowing forever.

TECHNIQUE OF ESOPHAGOSCOPY

In our department esophagoscopy is always carried out with the patient under a general anesthetic via the endotracheal route. For the newborn patient we use 4 or 5 mm full lumen Holinger or Jackson esophagoscopes, preferably with a built-in aspirating tube. Larger esophagoscopes are used for older children although we do not exceed an 8 mm full lumen esophagoscope.

The technique of esophagoscopy is the same as described by Jackson and Jackson.[20] We have the good fortune to have in our endoscopic operating room a multiplane fluoroscopy table and we find this of inestimable value in carrying out many of our procedures. Fluoroscopy combined with esophagoscopy is particularly useful in determining the level of a lesion being assessed. Spot roentgenograms may be taken where desired.

SUMMARY AND CONCLUSIONS

1. Although the anatomy of the esophagus is well known, there has been confusion regarding the epithelial lining at the lower end. Hayward[1] has coined the term "junctional epithelium" for it. The exact location of the cardia is also described.

2. Diseases of the lower end of the esophagus are described under the headings Congenital, Acquired Secondary to Congenital Defects, and Acquired.

3. Endoscopic diagnosis and evaluation as well as management of the diseases are discussed.

4. The technique of esophagoscopy in infants and children is briefly reviewed.

170 St. George St.

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LXXXIV

MALIGNANT MELANOMA OF THE ESOPHAGUS

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Malignant melanoma of the esophagus is a very rare lesion. Only 22 cases have previously been reported in the world literature as primary and two[1,2] as metastatic in the esophagus.

The purpose of this paper is to analyze the reported primary melanomas and to add an additional case thought to be primary.

REPORT OF A CASE

S.S., an 82 year old white female, was first admitted to St. David's Hospital on August 20, 1957, with the history of gradually increasing difficulty in swallowing and occasional regurgitation during the preceding eight months. She had had pain in the left anterior chest after swallowing for a period of four months. An electrocardiogram had been done and revealed no evidence of heart disease. A barium study May 30, 1957, had shown the presence of a non-obstructing, but space-filling polypoid lesion of the lower esophagus. The esophagus was dilated above the mass (Fig. 1). The possibility of a malignant tumor was considered at this time, but in view of the patient's age, her internist felt that she was not a candidate for resection of the esophagus. On the day of admission, the esophagus had suddenly become completely obstructed.

The past history was negative with the exception of a hysterectomy many years before.

The family history and review of systems was non-contributory.

Physical examination on the first admission revealed an elderly white female who was fairly well nourished, and who did not appear acutely or chronically ill. The skin was normal for her age, there being no lesions suspicious of melanoma. Careful examination of each system was negative with the exception of absence of the uterus. The liver was not enlarged.

The blood count revealed only a slight anemia at this time (hematocrit 39 vol. per cent; Hb. 11.3 gms).

An esophagoscopy was done on the second day of hospitalization. A moderate quantity of fluid was present in the thoracic esophagus. At a distance of 33.5 cm from the upper gum, a necrotic lesion was observed in the lower esophagus. A large mass of blue-black material, thought to be dark blood clots, completely filled the lumen of the esophagus. The esophagoscope could not be passed beyond this level into the stomach. A biopsy was taken from the left lateral wall of the esophagus.

Microscopy. Most of the biopsy material was composed of well differentiated squamous epithelium. Within the specimen was a focus, approximately one low power field in diameter, which was composed of malignant melanoma. The lesion was made up of pleomorphic anaplastic cells, many of which had giant nuclei. The cells were heavily pigmented with granular brown pigment. The lesion was covered with a segment of normal epithelium which in one small area exhibited melanin pigment (Fig. 2). The pathologic diagnosis was malignant melanoma.

Following the esophagoscopy, the patient was again able to swallow liquids until one week before her second admission, September 10, 1957. The blood count at this time revealed a marked anemia with hematocrit of 28 vol. per cent and a Hb. of 7.9 gms.

A tube gastrostomy was done on September 12, 1957, and a blood transfusion given. The patient was discharged from the hospital on September 24 and died at home on October 4, 1957. No autopsy was obtained.

Comment. Although no autopsy was obtained and the entire specimen could not be studied for evidence of a junctional change in the overlying epithelium, this tumor was considered to be primary in the esophagus for the following reasons: 1) there was no evidence of a primary lesion of the skin, orbit or other system, 2) this lesion was similar in its clinical pattern to that of other proven primary melanomas of the esophagus, and finally, 3) metastatic melanoma in the esophagus has been reported only one-tenth as frequently as primary melanoma.

REVIEW OF LITERATURE

Loring and Zeppa[3] collected 16 reported cases of malignant melanoma and added one of their own. These 17 cases were analyzed in the form of a very informative table. Loring and Zeppa omitted a case of melanosarcoma of the lower esophagus reported by Hof-

Fig. 1.—Barium study showing irregular polypoid lesion in distal end of esophagus, occupying almost the entire lumen.

mann,[4] cited by Keeley et al.,[5] who reported an additional case of primary melanoma of the esophagus. Ferro et al.,[6] Negre et al.,[7] and Fleming and Van Der Merwe[8] added another case each. The latter case was of particular interest in that the main portion of the tumor consisted of pale neurofibromatous tissue with a small central portion of melanoma in the stalk of the tumor.

CLINICAL FINDINGS

An analysis of the 23 reported cases brings to one's attention a striking similarity in the clinical course and pathologic findings of most of these melanomas of the esophagus.

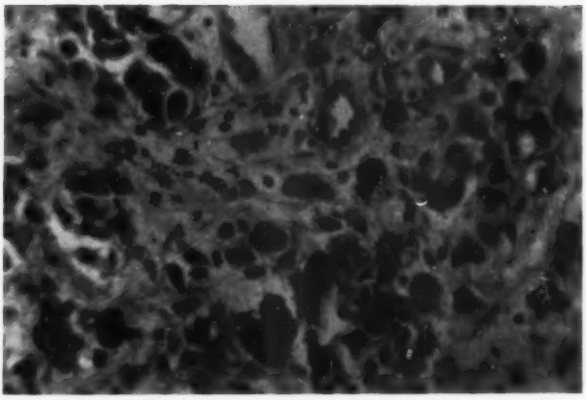

Fig. 2.—High power magnification showing large pleomorphic tumor cells with hyperchromatic nuclei and melanin pigment in cytoplasm.

The age of the patients varied from 40 to 82 years, with an average of 61.7 years for the entire group. Fourteen of the patients were males and nine were females.

The history in all cases was that of progressive dysphagia over a period of five weeks to twelve months, usually associated with substernal or epigastric discomfort or pain after swallowing. Weight loss was a constant symptom.

Physical signs were usually absent and laboratory findings were meager. Only two patients had occult blood in their stools.

A barium study was carried out in 18 patients and a filling defect was demonstrable in 16, often suggesting the nature of the lesion.

The diagnosis was established in each of the 23 cases by tissue examination; 12 by esophagoscopy and biopsy, 4 by study of the surgical specimen, and 7 by autopsy.

Grossly, from this compilation of cases, the typical lesion was a polypoid, lobulated, firm black tumor mass, varying in size from 3x2x1 cm to 11x13x13 cm. The tumor was located in the lower third of the esophagus in 12 patients, at the junction of the middle

and lower thirds in 5, in the middle third in 3, and in the upper third in 3 patients. It was attached by a pedicle in 18 of the total.

MICROSCOPIC FINDINGS

As stated by Loring and Zeppa[3] and others, the most striking characteristic is pleomorphism, there being a wide variation in the size and shape of the tumor cells. The tumors were classified as melanocarcinoma in most instances, but as melanosarcoma by four authors,[4,9,10,11] the distinction apparently being drawn on the basis of the type of cells predominating, and upon whether the pathologist considers melanoma to be of neuro-epithelial or of mesoblastic origin. Keeley et al.,[5] in view of the structural variation of melanomas, prefer the noncommittal designation of "malignant melanoma."

HISTOGENESIS

Melanomas arise from melanoblasts which of course do not normally occur in the esophageal mucosa. Allen[12] believed that melanoblasts may be derived from transformed basal epithelial cells that have undergone metaplasia and that pigment is formed in situ in these altered cells. Masson[13] proposed the theory that melanoblasts in the esophagus are misplaced (ectopic) dendritic cells that arise from the embryonic neural crest, and are accidentally deposited in the esophagus during embryonic development. Fleming and Van Der Merwe[8] state that the frequent association between neurofibroma and melanoma supports Masson's theory that melanoblasts originate in the neural crest.

A criteria for proving with certainty that a melanoma is primary at a given site was suggested by Allen,[12] who stated that one must be able to demonstrate a junctional epithelial change in the overlying or juxtaposed epithelium near the tumor. Allen and Spitz[14] broadened this concept to include visceral melanomas. This junctional change was demonstrable in seven of the reported cases.[3,5,15-19]

Robertson[20] observed that the expanding tumor may have destroyed the junctional change in the specimens in which it was not found. Loring and Zeppa agreed that Allen's requirement was not justified and included the 11 previously disputed cases[9-11,20-27] in their excellent review of the 17 cases reported by 1956. They pointed out that the junctional change requirement becomes further suspect when one considers the even more rare occasion in which the esophagus is the seat of the metastatic tumor.

TREATMENT

Melanomas have invariably been found to be resistant to irradiation.[28,29] Complete surgical excision, therefore, offers the only hope for cure.

In the esophagus, diagnosis of this tumor is always delayed, pending development of obstructive symptoms and one would expect the results of surgical treatment to be poor.

The esophagus was resected in 12 of the 23 reported cases. Of these, five patients were alive at the time of the respective case reports,[3,7,17-19] a period of six weeks to 12 months having elapsed postoperatively. Recent personal communication with four of these authors[3,17-19] revealed that 3 of the patients had died 8 months[17] and 12 months[3,18] after operation. Pomeranz and Garlock's[19,30] patient is still alive and well, 6½ years after resection of the esophagus!

In retrospect, it is interesting to note that this patient had obstructive symptoms for eight weeks before the diagnosis was made. The pedunculated lesion (6x3.5x2.5 cm) was located at the junction of the middle and lower thirds of the esophagus, and the muscular coat was not involved.

This one successful result proves that the prognosis for malignant melanoma of the esophagus is not entirely hopeless and should encourage those encountering this lesion in the future to select surgical excision as the treatment of choice if there is no gross evidence of metastasis.

SUMMARY

The 22 reported cases of primary malignant melanoma of the esophagus have been analyzed briefly and an additional case thought to be primary has been reported.

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LXXXV

BENIGN TUMORS AND CYSTS OF THE ESOPHAGUS

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Benign tumors and cysts of the esophagus are rare. Most specialists in gastroenterology see relatively few such lesions in their practices. For this reason it is well to review the clinical, roentgenologic, endoscopic, surgical and pathologic features of these lesions in order that they may be thought of when any unusual esophageal lesion is encountered.

Benign esophageal tumors have long been known to occur. Harrington[1] found that they had been recognized for some 200 years. They have been divided into two groups, depending upon where the major portion of the lesion presents in relation to the wall of the esophagus. The first group consists of benign pedunculated intraluminal tumors, and the second consists of benign intramural tumors. The pedunculated intraluminal tumors are exceedingly rare, yet they were the first to be recognized clinically because some were regurgitated into or beyond the mouth and were seen by the physician before the discovery of roentgen rays or invention of the esophagoscope. At times these tumors obstructed the larynx and caused death.

Moersch and Harrington,[2] in 1944, described 15 patients seen at the Mayo Clinic who had benign tumors and cysts of the esophagus, out of a total of 11,000 patients who had dysphagia. They pointed out that this constituted an inaccurate record of the incidence of these types of lesions, yet it gave an idea as to the incidence of these tumors among all lesions of the esophagus that produce symptoms. They reported also that up to that time, in 7450 postmortem examinations at the Mayo Clinic, 44 benign tumors of the esophagus had been found. None of these patients had had a history of esophageal difficulty. The microscopic diagnoses in these 59 cases were as follows: leiomyoma, 34 cases; hemangioma, four; polyp, four; papilloma, three; cyst, three; lipoma, two; adenoma, two; myxofibroma, one; fibrolipoma, one; neurofibroma, one; mucocele, one; and indeterminate, three. The three indeterminate tumors were thought, from

a clinical standpoint, most likely to be leiomyomas but microscopic confirmation was lacking.

Johnson[3] and associates, in 1953, reviewed the surgical experience of the Mayo Clinic with smooth-muscle tumors of the esophagus. Bernatz[4] and associates, in 1958, reported on six patients seen at this institution who had benign pedunculated intraluminal tumors of the esophagus.

To evaluate our most recent experience with benign tumors and cysts of the esophagus, we have reviewed the cases encountered here between the date of the report by Moersch and Harrington (1944) and January 1, 1960. Some of these cases were included in the reports by Johnston and Bernatz and their associates, but to give the experience of our last 15 years more validity, we have included them in the present analysis. During this period a total of 90 cases of benign esophageal tumors or cysts were encountered. In 49 cases the lesions were removed by surgical means, and in the other 41 cases the lesions were found at postmortem examination. In addition to these 90 cases, there were 26 cases in which a presumptive diagnosis of benign tumor or cyst was made by the roentgenologist and esophagoscopist, but these cases will not be included in this study because the diagnosis was not established by tissue examination.

SURGICAL CASES

The 49 benign esophageal tumors or cysts removed surgically included 33 leiomyomas, 10 cysts, one reduplication of the entire esophagus, two polyps, one lipoma, one pedunculated fibrolipoma and one pedunculated myxofibroma.

LEIOMYOMAS

Leiomyoma was by far the most common benign tumor of the esophagus, being observed in 22 men and 11 women. The average age of the patients was 43.6 years. The youngest was a girl of 13 years and the oldest a man of 68 years.

Size and location of leiomyomas are important considerations from the standpoint of diagnosis, treatment and results of treatment. For this reason we have divided the tumors into three groups: 1) leiomyoma 5 cm or less in diameter, 2) leiomyoma more than 5 cm in diameter yet not involving the stomach and 3) leiomyoma involving

the inferior portion of the esophagus and superior portion of the stomach.

Leiomyoma 5 cm or Less in Diameter. Sixteen patients were in this group. Twelve were men and four were women. Most of them had no symptoms referable to the esophagus and the tumor was found in these patients by the roentgenologist when he was investigating the upper part of the gastro-intestinal tract because of epigastric distress which was thought by the internist to be functional. In other cases the symptoms described were thought to be due to hiatal hernia or duodenal ulcer.

Six patients had dysphagia, two had experienced loss of weight, and one complained of "fullness" in the lower retrosternal region during the act of swallowing. Other symptoms described were "choking sensation," retrosternal burning, belching and salivation.

Roentgenologic examination of the esophagus was highly accurate. The lesion was seen roentgenologically in all but one case, and in 13 instances the roentgenologist said that benign tumor of the esophagus was the most likely diagnosis. In one instance a carcinoma of the esophagus was thought to be present. The defect was usually described as being well demarcated, oval or round, without evidence of ulceration.

Esophagoscopy was also highly accurate. The lesion was seen in all but one instance, and was reported as a benign esophageal tumor in all but one case. In this case the defect was so marked that a rhabdomyosarcoma was thought to be present. The leiomyoma that was not seen at the time of esophagoscopy was found at the time of operation for an associated esophageal hiatal hernia.

The findings on esophagoscopic examination are quite characteristic, namely a filling defect over which there is normal mucous membrane. The esophagoscope can be passed beyond the tumor without difficulty. A specimen should not be removed from the mucous membrane for biopsy, since this procedure could interfere with subsequent surgical removal. The surgeon can almost always shell out these tumors without breaking through the mucous membrane. A deep mucosal biopsy procedure could, at least theoretically, be responsible for esophageal leakage following surgical removal.

Surgical enucleation was performed successfully in all cases. Two patients had associated lesions. In one instance a hiatal hernia was

repaired and in another a carcinoma of the superior part of the stomach was removed. In the remaining cases the enucleation was without difficulty. Nine leiomyomas were in the lower part of the esophagus and seven were in midesophagus. In two instances multiple leiomyomas were found, one patient having three tumors and one having two. The results in all instances were regarded as excellent.

Leiomyoma More Than 5 cm in Diameter Without Involvement of Stomach. Most of these 13 patients had symptoms referable to the esophagus. These symptoms consisted of dysphagia, retrosternal pressure or burning, and flatulence, possibly due to aerophagia. There were twice as many men as women in this group. The results of surgical enucleation were excellent, provided it was not necessary to remove too large a segment of esophageal musculature in order to excise the tumor or tumors. The largest single tumor removed measured 17 by 13 by 8 cm and weighed 1070 gm.

Leiomyoma Involving Inferior Part of Esophagus and Superior Part of Stomach, Requiring Esophagogastrectomy. Three of the four patients in this group were young women, and one was a man of 51 years. As a group these patients presented more difficult problems in diagnosis, as well as in treatment, than did those in whom only the esophagus was involved. The results of treatment were, in general, far less satisfactory than in the first two groups. These tumors may give the appearance of achalasia at the time of roentgenologic and esophagoscopic studies.

CYSTS OF THE ESOPHAGUS

Cysts were the next most common benign lesion of the esophagus. Five of the 10 occurred in men and five in women. The average age of the patients was 45 years. Some patients had no symptoms referable to the esophagus, and some had dysphagia, "choking sensations," or vague retrosternal sensations. In most instances the esophagus was examined by roentgenography as part of a gastro-intestinal investigation for rather vague epigastric distress. All of these lesions occurred in the middle or the lower third of the esophagus. The surgeon was able to enucleate all of them. All patients had excellent results except one, who died on the thirteenth postoperative day with bilateral parotitis and cervical cellulitis.

COMPLETE REDUPLICATION OF ESOPHAGUS

Complete reduplication of the esophagus is a rare condition. It was represented by only one patient in this series.

This patient, a girl 18 years old, consulted her local physician because of cough. She had no symptoms directly referable to the esophagus. A roentgenogram of the thorax showed a posterior mediastinal mass. In roentgenograms of the thoracic part of the spinal column the mass was seen to contain calcium. Neither roentgenologic studies of the esophagus nor esophagoscopic examination was done, since the true nature of the lesion was not recognized prior to thoracotomy.

At operation, complete reduplication of the esophagus was found. Cystic structures were encountered at the junction of the lower and middle thirds. In addition, an anomalous artery was found arising from the thoracic aorta and supplying part of the lower lobe of the right lung. The esophageal reduplication extended from the pharynx and ran parallel, and was attached, to the esophagus. Dr. Stuart Harrington, who removed this structure, described it as having "the diameter of a little finger" in its superior portion but as increasing in diameter in its lowermost portion.

Pathologic examination revealed a tubular structure 17 cm long which was lined with stratified squamous epithelium. There were a submucosa and a muscularis mucosae. There also was smooth muscle in the wall of this structure and in places this was calcified.

The results of operation were excellent. Postoperative x-ray studies of the esophagus gave normal results.

POLYPS

The two esophageal polyps included in this series were removed at the time of esophagoscopy. Both were small tumors, one located in the distal part of the esophagus and the other at the cricopharyngeus level. The first patient had had no definite symptoms referable to the esophagus; the second had dysphagia for solid foods for 20 years. Both patients did well after removal of the polyps.

LIPOMAS

A lipoma measuring 6 by 1.5 cm was removed by enucleation at the time of right thoracotomy. It had occurred in a man 47 years of age who for 6 or 7 months had experienced an "irritation" under the superior portion of the sternum on swallowing solid foods. The x-ray and esophagoscopic findings were those of an intramural tumor. The patient did very well after operation.

PEDUNCULATED INTRALUMINAL TUMORS

Pedunculated intraluminal tumor is one of the most bizarre tumors that occur in the gastro-intestinal tract. Totten[5] and associates could find reports of only 40 such cases recorded up to 1953. Vinson's[6] report, in 1922, of the successful removal of this kind of tumor is the first such report to be found in the American literature. Bernatz and associates, in April, 1958, reported on six patients treated surgically at the Mayo Clinic. All but two of these patients had been reported on previously.

The most common clinical feature was esophageal obstruction. Thus, dysphagia, regurgitation, vomiting and considerable loss of weight occurred. Most patients had substernal distress which varied from a sense of fullness to pain that was suggestive of angina pectoris. Respiratory symptoms developed from aspiration of esophageal contents and at times from pressure on the tracheobronchial tree. Ulceration of the tumor may cause melena or hematemesis.

When regurgitation of the tumor into the mouth occurs, the diagnosis can be made without difficulty, provided it is thought of by the physician. Such regurgitation occurred in four of the six patients.

X-ray examination of the esophagus shows a dilated esophagus which may have the appearance seen in achalasia. The tumor may be mistaken for retained food or foreign material.

Esophagoscopy should furnish the diagnosis. At times, however, the esophagoscopist is fooled by finding the mucous membrane intact over the tumor. He may first recognize the tumor when he sees its distal end.

Treatment. Pedunculated intraluminal tumors should be removed surgically. Before the period of relatively safe transcervical or thoracic removal, some tumors were removed by cutting through the pedicle with a snare. There may, however, be fairly large blood vessels in the pedicle which would make this procedure somewhat hazardous. It is safest now to remove the tumor through either a transcervical or a transthoracic approach. If the tumor is not removed, the ultimate outcome in a large percentage of these patients is poor.

Laryngeal obstruction, aspirational pneumonitis and its complications, and esophageal obstruction with loss of weight may occur in

patients who have this type of tumor. Removal of the tumor usually gives complete relief of symptoms.

The two cases of pedunculated intraluminal esophageal tumor in our series were reported previously by Bernatz and associates, but for purposes of presenting the entire experience of the Mayo Clinic with benign esophagal tumors during the last 15 years, we have included them in this paper. The other four cases reported by Bernatz and associates were encountered prior to January 1, 1945, and for this reason are not included in our series.

REPORT OF CASES

CASE 1. *Pedunculated Fibrolipoma of Esophagus.* A woman, 25 years of age, who was admitted on March 27, 1955, complained of dysphagia of 1 year's duration. Food seemed to stick in her throat and it was necessary for her to take extra liquids to wash solid foods down. Her difficulty had gradually increased in severity and she had consulted her family physician in 1954. The physician thought her condition was of nervous origin. At Christmas time in 1954, she was unable to swallow solids, and regurgitated frequently. Although food stuck in her throat, it passed to the lower sternal region after she took liquids. She continued to take a liquid diet. She saw a nose and throat specialist on February 2, 1955, and after roentgenographic examination of the esophagus was told that she had cardiospasm. On February 5, 1955, an esophagoscopic examination was done and the esophagus was dilated under general anesthesia. She was able to take a soft diet for three or four days, and then her dysphagia again increased. Finally, she began to regurgitate liquids. She had lost 19 pounds since September, 1954.

Physical examination gave essentially negative results. The clinical impression was that of cardiospasm with a huge esophagus containing a bolus of food. The possibility of a phytobezoar was suggested. The roentgenologist suggested on examination that the possibility of funnel chest be excluded. X-ray examination was reported as showing cardiospasm with pronounced dilatation of the esophagus, and a large intraluminal foreign body that was 15 cm long.

On esophagoscopy the instrument passed into the lower part of the esophagus, which appeared to be of normal size, but there was no retention of material such as is characteristic of cardiospasm. As the lower parts of the esophagus was reached, the lumen suddenly widened and was seen to contain a large tumor. The esophagoscope was with-

drawn and then it could be inserted around the tumor in all directions. Finally, on withdrawal of the esophagoscope for a greater distance, a pedicle that contained fairly large blood vessels could be seen. It was believed that the tumor arose from the esophageal wall 10½ inches from the upper incisor teeth at approximately the level of the arch of the aorta; its origin seemed to be from the posterior wall, slightly more on the right than on the left. No biopsy specimen was taken.

At operation on April 2, 1955, the thorax was entered through a right posterolateral incision in the fifth intercostal space. The esophagus was found to be enlarged from the axygos vein down to just above the level of the diaphragm. It was opened longitudinally and a huge intraluminal tumor was encountered; this extended from just above the azygos vein, where it arose from a rather broad stalk, to a level just above the diaphragm. The tumor was delivered through the esophagus and the stalk was clamped and divided. The lower end of the tumor was somewhat ulcerated. The pathologist reported that it was a pedunculated fibrolipoma measuring 14 by 7 by 5 cm.

Postoperative studies of esophageal motility, on April 18, 1955, showed that the gastro-esophageal junction failed to participate in the swallowing reflex. No relaxation and no prolonged increase in pressure occurred. There was failure of the primary peristaltic waves. The results of a methacholine (mecholyl) test were apparently negative, although the patient did have some pain on being given this drug. The characteristics of achalasia were present except for failure of the esophageal pressure to rise during the methacholine test.

Motility studies on October 26, 1955, showed a change for the worse. The cardia seemed to be nonfunctioning and incompetent, and the patient appeared to have progressive nerve degeneration of the esophagus. Esophagoscopic examination on the same date disclosed a moderate amount of retained secretion in the esophagus. The esophagoscope was passed into the stomach without any evidence of obstruction. The examiner believed that there was some gastric mucous membrane above the level of the diaphragm. The esophagus was dilated to the caliber of a 50 F. sound.

According to a progress note made on October 24, 1955, the patient had done fairly well after operation until 4 weeks previously, when she began to have dysphagia quite similar to that prior to operation. She localized this at the cricoid level. She regurgitated food, and could swallow a full glass of water before regurgitation. She brought up a foamy type of secretion. Her weight had decreased

about 8 pounds in 4 weeks. Roentgenographic examination made on October 25, 1955, showed moderate secondary dilatation of the esophagus but without much delay in transit of food at the esophagogastric junction.

The patient wrote on February 14, 1957: "My health is very good. . . . My weight is low although my appetite is very good. I eat anything I wish. The only time I have an unpleasant sensation is when I eat and lie down too soon afterwards. I put several pillows under my head; this elevation relieves the uncomfortable sensation."

CASE 2. *Pedunculated Myxofibroma of Esophagus.* A man, aged 56 years, who was admitted August 6, 1951, gave a history of progressive anorexia, weakness, dysphagia, and loss of 48 pounds, of 6 months' duration. The illness had started with soreness in the right lower pharyngeal wall on swallowing. It was first noticed with the ingestion of liquor, then of hot foods, and finaly of cold foods. Each time he ate he experienced pain when the bolus of food passed the cricopharyngeus level. His local physician had found that the esophagus was very large. Esophagoscopic examination reportedly had given negative results. Finally, he had had so much pain on swallowing that it was necessary to put a Levin tube into the stomach.

Physical examination on admission gave negative results except for evidence of weight loss. The roentgenographic appearance of the thorax was normal. The roentgenologist reported the presence of a large intraluminal mass in the mid portion of the esophagus, possibly an intramural tumor, a large collection of food or an intraluminal tumor. He did not find too much evidence of obstruction at the esophagogastric junction and did not believe that cardiospasm was present.

Esophagoscopic examination revealed a large pedunculated tumor that arose just below the esophageal introitus from the posterior and left lateral walls of the esophagus. From this point it hung down into the lumen of the esophagus, extending into the lower third. The tumor was lobulated and was thought possibly to be bifid. The examiner was able to grasp the lower end of the tumor but he could not bring it out of the mouth because it was so tightly embedded. His impression was that of a large pedunculated intraluminal fibrolipoma. The pathologist reported the tissue to be esophageal mucous membrane.

An operation was performed on August 11, 1951. An incision was made along the anterior border in the sternocleidomastoid muscle

on the right, and a longitudinal incision was made in the right lateral wall of the esophagus just below the introitus. The pedicle of a large intraluminal esophageal tumor arising from the left lateral wall of the esophagus was found. This pedicle was 1.5 to 2 cm in diameter. It was cut across and closed with interrupted stitches. The pathologist reported that the tumor was a pedunculated myxofibroma measuring 12 by 5.5 by 4 cm, with the pedicle measuring 11 by 2 by 1.5 cm. A roentgenogram of the esophagus made on August 21, 1951, did not show any abnormality.

The patient wrote on June 19, 1956, that he had no difficulty in swallowing.

BENIGN TUMORS AND CYSTS FOUND INCIDENTAL TO POSTMORTEM EXAMINATION

Forty-one benign tumors and cysts of the esophagus were found incidentally at the time of postmortem examination. All of these were so small that they did not cause any symptoms. The 41 lesions consisted of 24 leiomyomas, 13 cysts, one lipoma, one submucosal fibroma, one adenoma, and one lymphangioma.

SUMMARY

A total of 90 patients with benign esophageal tumors or cysts were observed at the Mayo Clinic in the 15-year period from January 1, 1945, through December 31, 1959. In 49 of these patients the lesions were removed surgically, and in 41 they were found incidentally at the time of postmortem examination. The types of tumors and the clinical features are described.

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LXXXVI

PULMONARY VENTILATION THROUGH THE BRONCHOSCOPE

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In the vast majority of cases requiring bronchoscopy airway obstruction is unilateral due to a foreign body below the bifurcation, or bilateral due to impaired bronchial drainage. The existing primary airway obstruction will generally determine the amount of resistance opposing pulmonary ventilation before passage of the bronchoscope. The degree of airway obstruction frequently regulates the arterial tensions of oxygen and carbon dioxide.

The patient with obstructed airways or impaired mechanical function of the pulmonary system can be free of cyanosis when he is breathing supplemental oxygen. This fact can obscure a rapidly progressing respiratory and metabolic acidosis. If a patient who is scheduled for bronchoscopy has been receiving supplemental oxygen in a tent or by catheter he may be in a serious state of carbon dioxide narcosis. Any additional insult to the patency of his airway could lead to rapid pulmonary collapse. This patient usually displays a rapid shallow diffusion type of spontaneous respiration. When supplemental oxygen is withdrawn, depth of respiration may increase with increasing signs of dyspnea.

The pathological physiology in this type of patient could be a respiratory center depression caused by the elevated arterial carbon dioxide tension which follows airway obstruction. When arterial oxygen saturation falls to approximately 93 per cent, the carotid chemoreceptors take over a major part of respiratory control. When the carotid chemoreceptors are inactivated by a rising oxygen tension in the inspired air the minute pulmonary ventilation decreases. Alveolar minute ventilation falls also and a rise in alveolar and arterial carbon dioxide tension quickly occurs.

A logical approach to therapy in this type of patient would be the use of positive/negative pressure breathing before bronchoscopy. This form of therapy simultaneously increases the arterial oxygen

saturation while decreasing the arterial carbon dioxide saturation. This is accomplished by increasing the minute alveolar air exchange, which blows off carbon dioxide while oxygen tension increases. This provides the bronchoscopist with a patient who has greater initial pulmonary reserve.

The positive/negative respirator should be set up to provide a fifteen minute pulmonary therapy period immediately before insertion of the bronchoscope. This can be accomplished through a mask, mouthpiece, or endotracheal tube either by assisting, or by controlling respiration. A positive inspiratory pressure limit of from 15 cm H_2O to 25 cm H_2O is usually adequate. Begin with the 15 cm H_2O setting. A negative pressure limit of 3 cm H_2O is adequate and should not be exceeded. Inspiratory flow rate should be slow enough to allow adequate time for gases to flow through the narrowed airways. The inspired gases should be moistened by a nebulizer which contains 5 drops of 2.25% racemic epinephrine, and 60 drops of 20% ethanol. The expiratory phase should be timed so that it is equal or longer than the inspiratory phase to bring about a reduction in functional residual capacity.

If a bronchoscope with a side arm connection for oxygen is inserted into the airway, pulmonary ventilation can be maintained during bronchoscopy by connecting the bronchoscope side arm to the same positive/negative pulmonary respirator used earlier to prepare the patient for bronchoscopy.

It must be remembered that the existing ventilatory embarrassment will be further insulted by any additional encroachment upon the airway. When the additional resistance created by the effective decrease in radius and increase in length of the trachea due to insertion of the bronchoscope is superimposed upon existing elevated airway resistance, ventilation may be impeded enough to kill the patient.

Connecting a constant flow of oxygen to the side arm of the bronchoscope and capping the proximal end of the bronchoscope makes possible a pressure gradient of 10 to 60 cm H_2O between the bronchoscope and the alveoli which causes oxygen to flow into the lung. This method, however, does not provide for a reverse pressure gradient to enhance the flow of gases out of the lung during the expiratory phase of respiration. A positive/negative pressure respirator must be used for this purpose. However, until recent technological advances allowed more flexibility in designing mechanical ventilators such devices were not applicable for use during bronchoscopy.

The limiting factors were: 1) the inability of volume limited pumps to ventilate the patient who had varying leaks in his airway connections, and 2) the rapid rise in pressure in the upper airways causing premature cut off of the inspiratory phase in the pressure limited respirators. With neither respirator could alveolar ventilation be maintained at desirable levels.

An ideal positive/negative pressure respirator provides for: 1) a manually adjustable inspiratory flow rate with a pneumatic clutch to allow a low mean pressure gradient between the proximal airway and the distal lung. This allows time for inflowing gases to overcome the existing resistance to inspiration, otherwise a rapid buildup of pressure in the proximal airway switches the respirator off at the pre-set pressure limit before the desired tidal volume has been delivered into the lung; 2) an adjustable negative pressure limit which allows control of the rate of flow of gases from the tracheobronchial tree during expiration. This provides a means of reducing the expiratory resistance to flow, thus reducing re-breathing from dead space, and possibly enhancing venous return to the right heart; 3) a means for assisting spontaneous respiration and controlling ventilation in the apneic patient. This prevents the patient from "bucking" against the respirator and allows relaxants to be used to control compliance of the thoracic cage and prevent spasm of the cords, etc.; 4) intermittent nebulization to drop resistance in the peripheral airways.

All important is the fact that with adjustable inspiratory and expiratory flow rates satisfactory ventilation can be carried out through the narrowest and the widest airways. To resume ventilation at any point during bronchoscopy basically all that has to be done is to re-cap the proximal end of the bronchoscope and adjust the inspiratory flow rate until desired tidal exchange is obtained.

The only contraindication to this form of ventilation through the bronchoscope is (as is the case for most general procedures) lack of knowledge concerning the mechanical respirator and the physics of gas flow.

SUMMARY

The modern mechanical ventilator incorporating technological advances designed by the engineer for the physician allows the bronchoscopist further improvements in his procedures.

212 Cerritos N. W.

LXXXVII

INTRATRACHEAL GOITRE

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The first case of intratracheal goitre was reported in the German literature in 1875 by Ziemssen who treated a thirty year old male whose chief complaint was dyspnea. The patient suffered from an intratracheal tumor measuring 2x1x1 cm which communicated at the level of the cricoid cartilage with an exterior nodular goitre. The first successful resection of this lesion was performed by Heisse in 1888, on a 25 year old German male who had an intratracheal tumor at the level of the first tracheal cartilage. The lesion was dealt with by tracheal fissure and curettement. The first mention of this lesion in the American literature is by Freer in 1901, who described the lesion in a thirty-two year old female whose intratracheal tumor was treated by endoscopic coagulation, with tracheostomy required. Theisen, in 1902, observed a thirty-five year old female with an intratracheal lesion which produced dyspnea and which was treated by tracheal fissure.

The sporadically occurring reports in the literature are similar in content and implication and the story is a repeated one, of patients, usually young, complaining of dyspnea and presenting, on physical examination, an intratracheal or intralaryngeal tumor, the surgical management of which is fraught with some degree of difficulty.

The present case is of a thirty-eight year old Negro female who was admitted to the University of Alabama Medical Center with a history of hemoptysis for two days prior to admission. Within the past several months, she had had two previous episodes of hemoptysis. Her past history revealed a thyroidectomy for nodular goitre, thirteen years prior to the present admission. Respiratory wheezing accom-

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panied a chronic cough for the two years preceding admission. Physical examination revealed a well-healed thyroidectomy scar under which a nodular mass could be palpated. The breath sounds were described as distant and wheezing in both lungs. Since the differential diagnosis encompassed the so-called bronchial "adenoma," bronchiectasis and tuberculosis, bronchoscopy was undertaken in an effort to resolve the differential. At bronchoscopy, a subglottic mass measuring approximately 1.5x1.5x1.0 cm was visualized. This was biopsied and the surgical pathologist returned a report of aberrant thyroid tissue. The patient subsequently developed severe laryngeal edema and hemorrhage requiring tracheostomy for relief. Brisk hemorrhage occurred through the tracheostomy tube and it was decided to excise the thyroidectomy scar and the nodule underlying it. The surgical pathology diagnosis on this tissue was nodular goitre. Recurring hemorrhage was a problem, requiring constant tracheal suctioning and transfusions of some fifteen units of blood. For these reasons, an emergency tracheal fissure was performed. The laryngectomy specimen showed thyroid tissue extending from the exterior across the cricothyroid and tracheal ligaments into the tracheal lumen. The tumor measured approximately 2x2x1 cm and, histologically, it was noted that the struma spared the cricoid cartilage and the tracheal rings. The intratracheal portion was invested by intact mucosa, save at the site of biopsy where the mucosal investment was missing.

The histologic picture of the mass was that of a nodular goitre and there was no morphologic evidence of malignancy.

Fewer than ninety cases of intratracheal goitre are recorded in the literature and the majority of these reports are in the German literature. Less than a dozen instances are recorded in the English literature. From the literature, it is apparent that this condition is observed most frequently in the third and fourth decades and, like all thyroid diseases, is more frequent in females than in males. All previously recorded cases have been in the Caucasian race but this is interpreted as a reflection of the area from which most of these cases were deriverd. Since the histologic pattern is that of a nodular goitre, it is expected that it would be more frequently observed in the endemic goitre zones. That such is the case is well borne out by the literature. Approximately three-quarters of the recorded instances have been associated with external goitres. The external goitres, moreover, serve as a complication in the diagnosis and management of intratracheal goitre. First, the intratracheal goitre may be evident only years after the resection of the external nodular goitre. Secondly, the mere presence of the external goiter may obscure the true cause of the dyspnea of which so many of these patients complain.

Since external goitres may produce dyspnea, it has been assumed in many of these reports of intratracheal goitre cases, that the external goitre was the sole cause of the dyspnea.

The symptoms and signs of intratracheal goitre are related to a space-occupying lesion in the respiratory lumen. Small lesions may, indeed, be asymptomatic but, in general, the principal symptom is dyspnea. From the literature, it is apparent that the average duration of dyspnea before diagnosis is some five years. The range, however, is marked and in Ziemssen's case, it was present for only a few weeks before diagnosis; whereas Wurster reported an instance in which dyspnea had been present for twenty-seven years prior to diagnosis of intratracheal goitre. The dyspnea varies cyclically with menses and pregnancy and may become so marked with menstruation as to be complicated by sudden asphyxia; the same situation obtains in pregnancy. Pregnancy is, moreover, no complication to therapy. In some individuals, inspiratory stridor and thrill have been recorded, and in a few instances, the dyspnea has been so marked as to be accompanied by intercostal retraction and cyanosis. It is interesting that, including the present case, hemoptysis has been recorded in only five patients.

The clinical differential diagnosis is that of any intratracheal tumor, which would include both the benign and malignant neoplasms, the reactions to injury, and the truly inflammatory conditions. The surgical pathologic differential diagnosis would, in general, embrace only three conditions, namely well-differentiated follicular carcinoma of the thyroid, primary hyperplasia of the thyroid, and cylindromatous carcinoma. In resolving the surgical pathologic differential diagnosis, the only difficulty which should be encountered would be in the case of the well-differentiated follicular carcinoma, which may present great difficulties in precise classification.

A review of the pathologic features described in the literature shows the incidence of malignancy in intratracheal goitre to be approximately 11%. However, in the light of present day knowledge it is not possible to accept as cancer all cases so designated in the past. In part, this is related to an archaic terminology which has little meaning in terms of present day surgical pathology practice, and, in part, is a reflection of a change in concept of thyroid malignancy. However, a review and reclassification, according to current concepts, would show an approximate rate of malignancy of 7%. This is to be compared with a 3% incidence of malignancy in surgically resected thyroids examined in various clinics over this country. The patho-

logic diagnosis, moreover, rests ultimately on an awareness of the condition.

The thyroid primordia develops at an earlier stage in embryonic life than do the tracheal cartilages which are not complete until the 43 mm stage, while the separation of the pharynx from the lateral thyroid lobes occurs at the 18 mm stage. This tracheal lag permits separation and intratracheal sequestration of primordial portions of the lateral lobes. Failure of fusion of the ultimobranchial bodies with the medial thyroid primordia permits the explanation of central, aberrant thyroid tissue, remote from the external gland. Thus, it would seem that there are several distinct embryologic possibilities for aberrant thyroid tissue to be found. Pathologists have encountered aberrant thyroid tissue in the pericardium and in the mediastinum, extending to and involving the pleural aspect of the diaphragm. On the basis of the literature, and the present case, we must include, as embryologic possibilities for aberrant thyroid tissue, intratracheal and intralaryngeal locations. The so-called "lateral aberrant thyroid" remains an embryologic impossibility and in virtually all instances, is related to an occult follicular carcinoma of the thyroid.

The therapy of intratracheal goitre is, by and large, surgical. In fact, when respiratory embarrassment occurs, there is little place for the non-surgical management of this condition. An endoscopic approach may be warranted at the level of the cords but a laryngeal or tracheal fissure is possibly most satisfactory. It is important to consider tracheostomy as a primary maneuver in the surgical therapy and to avoid open biopsy because of the dangers of attendant hemorrhage. Extramucosal curettement has been instituted in a number of instances with success, and strangely enough, the recurrence rate in patients treated by this admittedly non-ablative procedure, has been remarkably low.

In summary, intratracheal goitres are an unusual cause of respiratory obstruction. The great bulk of case reports is to be found in the German and French literature and infrequently in the English-speaking literature. The correct management of this condition, which is quite amenable to appropriate therapy depends upon:

a) Clinical awareness of the condition
b) Avoidance of open biopsy
c) Education of the pathologists.

The pathogenesis of this rather bizarre and interesting condition relates to the development of the thyroid and trachea.

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LXXXVIII

INOPERABILITY OF CARCINOMA OF THE LUNG ESTABLISHED BY CARINAL BIOPSY

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Information referable to operability of pulmonary cancer is of obvious primary interest to the thoracic surgeon. In a particular case the degree of proximal extension of the tumor frequently constitutes a very difficult question to answer. Physical, roentgenological, and bronchoscopic examinations may fully justify a good prognosis but histological examination of the surgically removed lung not infrequently reveals a more extensive proximal spread of the tumor and inadequate excision of same.

Griess, MacDonald and Claggett's[1] studies revealed a high percentage of extension of the tumor in the bronchus proximal to the macroscopic limits of the cancer. Such proximal microscopic extension was observed in 62% of the cases of squamous cell epithelioma and in 50% of those with adenocarcinoma. These microscopic extensions ranged from 0.3 mm to 20 mm. The authors therefore recommended severing the bronchus more than 20 mm from the gross limits of adenocarcinoma while 15 mm was considered as a safe distance for squamous cell epithelioma. Another equally important conclusion of these authors concerned the type of spread of the tumor. The most frequent extension of the tumor involved the outer fibrous coat of the bronchus. The mucosal layer was involved less frequently. The submucosa was found to be the least frequent site of extension. This excellent study added much to careful planning of cancer surgery of the lung.

Attention was called to the importance of lymphatic spread of carcinoma of lung by Rabin, Selikoff and Kramer.[2] They reported 16 cases in which the paracarinal region appeared grossly normal yet microscopic examination of the biopsy from the same region disclosed submucosal lymphatic extension of the tumor which originated more

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Presented as candidate's thesis for the American Broncho-Esophagological Association.

distally. Such occurrence represented approximately 10 per cent in their series of cases of proven carcinoma of the lung. They felt the routine biopsy of paracarinal mucosa was of definite importance in the evaluation of operability of the patient. Paracarinal biopsy revealed microscopic extension by tumor in 16 per cent of the patients who otherwise appeared to be good subjects for cure by pneumonectomy.

The present study was undertaken to throw further light on the proximal spread of pulmonary cancer. Twelve consecutive cases were studied in detail. Superficial biopsy from the homolateral side of the carinal mucosa was taken in each instance. Only cases with macroscopically normal bronchial mucosa between tumor and carina were analyzed in the study. The distance between the peripheral lesion and carina exceeded 25 mm in all cases. First the biopsy from the carina was taken with cup forceps following which a separate forceps was used for biopsy of the peripheral lesion. This sequence may be of importanec in order to avoid contamination of the carinal biopsy by exfoliated tumor cells.

REPORT OF CASES

CASE 1. A 51 year old male was bronchoscoped for a hilar mass on the right side discovered by x-ray studies. Examination revealed a normal tracheobronchial tree. Biopsy from the carina revealed tumor cells present only in the lymphatics (Figs. 1 and 2). The mucosa was normal. A blind biopsy was taken from the orifice of the right lower lobe which revealed microscopic submucosal infiltration and lymphatic permeation by squamous cell epithelioma (Figs. 3 and 4).

CASE 2. A 63 year old male. Bronchoscopic examination: the orifice of the left upper lobe bronchus was stenosed by slightly papillary mucosa. This was visualized by means of the right angle telescope. The remaining bronchial tree was normal except for questionable widening of the carina, motility of which was normal. Biopsy was first taken from the carina which revealed the lymphatics filled with oat cell tumor. No tumor cells were found in the mucosa. Biopsy from the orifice of the left upper lobe bronchus revealed oat cell carcinoma with diffuse, subepithelial infiltration.

CASE 3. A 58 year old male. Bronchoscopy revealed a greyish, broad based swelling about 10 mm proximal to the orifice of the right middle lobe bronchus. The carina appeared grossly normal. Biopsy from the carina showed tumor cells in the lymphatics. The tumor

Fig. 1.—Case 1. Carinal biopsy. Lymphatic permeation (L). Remainder of the specimen is free of malignant cells. (X115)

did not extend to the mucosal surface. Biopsy of the lesion in the right main bronchus showed undifferentiated squamous cell epithelioma with lymphatic permeation. Tumor cells extended to the mucosal surface.

CASE 4. A 57 year old male. Bronchoscopy revealed a normal tracheobronchial tree. However, examination with the right angle telescope showed compression of one segmental orifice of the right upper lobe. Biopsy from the carina showed epithelioma in the submucosal lymphatic spaces without any evidence of tumor on the mucosal surface. Biopsy from the orifice of the right upper lobe, in an area which grossly appeared normal, showed lymphatic permeation by tumor cells without evidence of extension to the mucosal surface.

CASE 5. A 54 year old male. Bronchoscopy: tumor found to be protruding from the orifice of the right upper lobe bronchus. The carina was normal in appearance and motility. Biopsy from the carina revealed adenocarcinoma in the lymphatics and interstitial infiltration of the submucosa. Biopsy from the tumor of the right upper lobe bronchus showed infiltration of the submucosa and lymphatics.

CASE 6. A 57 year old male. Bronchoscopy: stenosis of the left upper lobe bronchus was visualized with the right angle telescope.

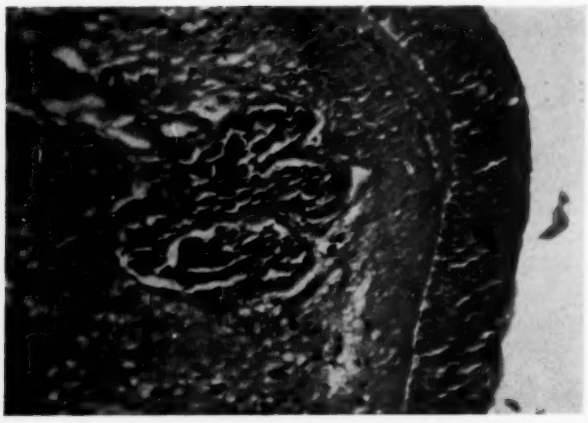

Fig. 2.—Case 1. Lymphatic permeation under high power (X270). Squamous cell epithelioma in spaces lined by endothelial cells (E).

The remaining tracheobronchial tree including carina was normal. Biopsy from the carina revealed no tumor. Biopsy from the orifice of the left upper lobe bronchus revealed squamous cell epithelioma infiltrating the entire mucosa. The lymphatics were permeated by tumor cells. At thoracotomy the tumor was found to invade the heart.

CASE 7. A 51 year old female. Bronchoscopy: a tumor was visible through the right angle telescope in the right upper lobe bronchus. The carina appeared normal. Biopsy from the carina failed to reveal the presence of tumor. Biopsy from the orifice of the right upper lobe bronchus showed squamous cell epithelioma with heavy infiltration of the entire mucosa including its surface.

CASE 8. A 72 year old female. Bronchoscopy: a small tumor was found in the most distal portion of the right main bronchus. The rest of the tracheobronchial tree was normal. Biopsy of the carina did not contain tumor cells. Biopsy from the right main bronchus showed poorly differentiated squamous cell epithelioma most of which was found to be subepithelial in location.

CASE 9. A 63 year old male. Bronchoscopy: a papillary tumor was found 15 mm distal to the orifice of the right upper lobe bronchus. The remaining tracheobronchial tree was normal. Biopsy from

Fig. 3.—Case 1. Biopsy from right lower lobe bronchus. Lymphatic permeation (L). (X115)

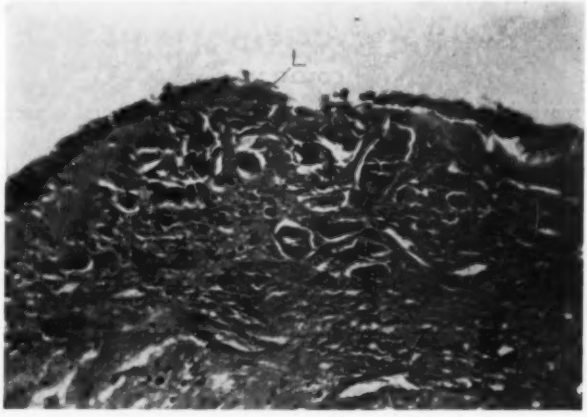

Fig. 4.—Case 1. Biopsy from right lower lobe bronchus. Epithelioma cells in lymphatics (L). (X270)

the carina revealed no tumor. Biopsy from the right main bronchus revealed the entire specimen to be heavily infiltrated by squamous cell epithelioma.

CASE 10. A 44 year old male. Bronchoscopy: an exophytic tumor in the right main bronchus was found 5 mm distal to the orifice of the right upper lobe. The carina appeared normal. Biopsy from the carina showed no tumor. Biopsy from the exophytic lesion revealed squamous cell epithelioma with ulceration and extensive infiltration of the entire specimen by tumor cells.

CASE 11. A 61 year old male. Bronchoscopy: minimal stenosis of the right lower lobe bronchus. The rest of the tracheobronchial tree was normal. Biopsy from the carina did not reveal evidence of tumor. Biopsy from the right lower lobe bronchus showed adenocarcinoma with peribronchial spread. Pneumonectomy was performed. Microscopic studies revealed adequate excision.

CASE 12. A 77 year old male. Bronchoscopy: no endobronchial growth was found but there was extrinsic compression of the right upper lobe bronchus. Biopsy from the carina revealed no tumor. Biopsy from the right upper lobe bronchus showed nondifferentiated squamous cell epithelioma without invasion of the mucosal surface.

COMMENT

Superficial biopsy was taken from the homolateral aspect of the carina in 12 consecutive cases in which normal bronchial wall separated the site of the peripheral biopsy from the carina. Carinal biopsy revealed the presence of malignancy five times out of 12. In these five cases the primary tumor was locatd in the right lower lobe bronchus in one case, at the right middle lobe bronchus in one case, in the right upper lobe bronchus in two cases, and in the left upper lobe bronchus in one case. The histological characteristics of the tumor taken from the primary site were identical with those of the carinal biopsy in each of the five cases. A prominent feature in these five cases was the finding of lymphatic involvement in both the carinal biopsy and biopsy of the primary lesion. In several instances it was evident that the only tumor cells present in the specimen were localized to the lymphatics while the overlying mucosa was normal (Figs. 1 and 2). In the six patients who had negative carinal biopsies, lymphatic permeation of the primary lesion was not observed in the biopsy specimen. In this group neoplastic infiltration of both submucosa and mucosa was present.

In one case, although the carinal biopsy was negative, lymphatic permeation of the primary lesion was present. At thoracotomy this case proved to be inoperable.

It would seem advisable to take a carinal biopsy in every patient being considered for pneumonectomy. If the carinal biopsy is positive, then surgery could be only palliative. If the carinal biopsy is negative, then the biopsy of the primary lesion should be carefully examined for the presence of lymphatic involvement. If lymphatic permeation is found, then, in view of the above material, it is quite likely that similar pathology is present at the carina but escaped detection by biopsy. This is bound to occur since the carinal mucosa is grossly normal and the biopsy is thus taken "blindly."

Finally it should be added that no complications resulted from carinal biopsies in this series.

SUMMARY

1. A significantly high percentage of biopsies taken from the carina of patients with carcinoma of the lung revealed the presence of malignant cells in the lymphatics although large segments of macroscopically normal mucosa separated the carina from the primary tumor.

2. In each case where the carinal biopsy was positive, lymphatic permeation by malignant cells in the biopsy taken from the primary tumor was found.

3. Routine carinal biopsy adds to the proper selection of those cases suitable for surgery.

4. If the lymphatics in the biopsy of the primary lesion are involved, the prognosis after radical surgery is probably poor, even though negative carinal biopsy was obtained.

180 FORT WASHINGTON AVE.

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LXXXIX

BRONCHOSCOPY IN THE TREATMENT OF LUNG CANCER

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This is a study of 42 patients with primary or secondary cancer of the lung that were treated with radio-active isotopes bronchoscopically. No attempt is made to claim that this is a primary method of treatment in the majority of cases but a review of this material shows that there are certain inherent values in such treatment as an adjuvant method to the surgical and more usually employed radiotherapeutic methods available to us. There 42 patients have been treated since 1946 except for one instance treated 10 years earlier.

The method of treatment has consisted of either the application of a capsule containing radon against a surface area within the tracheobronchial tree or by the actual implantation of radon seeds through the wall of the trachea or the bronchus. The capsule in question may be 3 cm or 4 cm in length, consists of an outer shell of polyethylene 2 mm in thickness and inwardly contains radon gas in glass capillary tubes. These glass capillary tubes are contained in platinum jackets 2 mm in wall thickness to provide filtration. Strength of the contained capsule can be varied and it has been customary to use 50 or 60 millicuries in the two peripheral capsules and slightly weaker capsules medially to provide an even distribution. The over-all diameter is 6 mm and to the haft of the capsule is attached a malleable steel wire 100 cm in length or double the length of the bronchoscope and sufficiently firm to hold the capsule in place. The radon seeds are those described by Failla and employed for many years in various tumor sites by Martin, Watson, Pack and others. The strength of the individual seed varies from 0.7 to 1.5 millicurie. The wall is gold capillary tube .008 mm in diameter. Introduction is made through a 19 gauge needle with a bevelled sharp point and a stylet which extrudes the seed into the adjacent tissue.

Within the thorax implantation of radon seeds at thoracotomy where a resection for primary lung cancer proved impossible has been

employed for 18 years and was first reported on by Binkley. Considerable palliation has been achieved and some salvage of more than ten years has been encountered at thoracotomy with this method as the sole treatment. In the series of cases to be reported, the endobronchial treatment has been usually employed at a time when other methods have failed or been contra-indicated.

CONTRA-INDICATIONS TO BRONCHOSCOPIC USE OF RADIO-ISOTOPES

The contra-indications to the use of this method are first of all general contra-indications to any bronchoscopy such as drug sensitivity, cardiac failure or severe asthma or severe ventilation impairment due to emphysema, radiation pulmonary fibrosis or extrinsic fixation of the trachea or bronchus by carcinomatous infiltration. In the instances where the tracheobronchial tree is severely fixed by the encroachment of the cancer on the outer surface of the hollow viscus and ventilation has been severely impaired, the addition of the medication necessary for bronchoscopy may precipitate an irreversible respiratory embarrassment.

On the other hand, where the disease is endobronchial in major extent with obstructive phenomenon due to the endobronchial disease then an ideal situation is present for the use of one or the other methods above described.

TECHNICAL CONSIDERATIONS

In the eight cases in which the capsule was used a successful placement was achieved in seven. In one patient who had previously had thoracotomy with radon implantation and external irradiation and was showing some two years later a severe cough with hemoptysis and evidence of recurrence within the left main bronchus as proven by biopsy and bronchial washings and sputum studies by Papanicolaou technique the capsule would not remain in place but was coughed up. There was no evidence of laryngeal damage by the wire.

Complications that may occur with the seeds are first of all migration from the site of election. The placement of the radon seed is into tumor tissue as the holding structure and this tumor tissue may be visible through the bronchoscope as endobronchial tumor and if the placement is to be made in tumor outside the bronchial wall then this must definitely be evident as a fixed area subjacent to the endobronchial spread. It has not been our practice to introduce

the needle more than 1½ cm into the tumor and certainly no further than this in the tumor on the outer surface of the tracheobronchial wall. This depth is gauged by observing the haft of the needle at the ocular end of the bronchoscope at the time the tip of the needle is passed through the mucous membrane. The seed may be placed in too shallow position and dislodged by coughing or suction. In such instances it usually passes to a dependent position in the air passages and in our experience with several such situations there has been no demonstrable damage to the normal bronchial mucosa or adjacent lung parenchyma and in such an instance at autopsy, the seed lies encased in scar tissue. At the end of one of these procedures with radon seeds the suction apparatus should be monitored with a Geiger counter in case a seed has been aspirated into the suction unit. The second complication to anticipate is hemorrhage from the introduction of radon seeds. We have seen in interstitial implantation of radon seeds at open thoracotomy two rather alarming instances of endobronchial hemorrhage in 323 such implantations. In both instances the bleeding stopped and the situation was kept under control by adequate tracheobronchial aspiration. In the 42 endobronchial cases there has been no such important complication. It is well to point out however that the taking of biopsy from tumor, particularly carcinoid or cylindromatous tumor of the major air passages, or a deep bite in the carina particularly at the entrance to the right middle lobe, may lead to serious endobronchial hemorrhage.

There has been a question as to whether the introduction of seeds through the wall of the bronchus could produce peribronchial abscess or fistula. The introduction of radon seeds in the bronchial stump after pulmonary resection for cancer with local recurrence has been carried out in ten instances and in one such instance there was definite evidence of a local abscess or local empyema at the stump apex but this area was associated with persistent and uncontrollable epidermoid carcinoma so that the relative importance of the radioactivity and the penetration of the bronchial mucosa and the persistent cancer in producing the local infection cannot be properly assayed.

The most major complication to radon seed implantation and also to capsule treatment of the major bronchi has been radiation reaction in the esophagus. A severe esophagitis can be produced as this organ is very close to the left main stem bronchus and very sensitive to radiation effect. There have been several instances of transient dysphagia and two instances of esophagitis with dysphagia for three or four months after radon seed implantation. The employment of a bland diet and the use of Oxaine and one-half per cent Pon-

tocaine® in Amphogel® has been helpful in allowing the patient to maintain nutrition. Finally, poor judgement should be listed as a complication of this modality. In addition to the 42 cases reported, there were two deaths in patients who were being bronchoscoped for seed implantation but in neither of whom was it possible to employ the desired technique. Both of these patients had recurrence after pneumonectomy with encroachment upon the entrance to the remaining main bronchus and in both the bronchoscopy precipitated a serious crisis in respiratory deficit in patients already with ventilation embarrassment.

INDICATIONS FOR THE USE OF ENDOBRONCHIAL RADIOACTIVE ISOTOPES AND RESULTS OF SUCH TREATMENT

1. A simple indication for the use of radon seeds through the mucosa of the tracheobronchial tree is as a marker for exact localization of external irradiation. There are instances of cancer in the major tracheobronchial tree which do not show well on radiograph and which are not amenable to surgery and in such instances the placing of an inactive radon seed at the center or at the margins of the visible tumor will aid in the accuracy of the radiotherapist's attack on the neoplasm.

2. As an adjunct to external irradiation this modality was used in 22 patients. There seldom was any demonstrable aid over the course run by patients without adjuvant and no statistically demonstrable increased longevity. There was one unusual patient in whom this method did appear to be particularly helpful. This woman (E.L.) who previously had successfully been treated for carcinoma of the bladder and carcinoma of the rectum, appeared with a three months' history of hemoptysis and cough and was found to have total atelectasis of the left lung. At bronchoscopy a tumor mass in the left main stem bronchus was identified which was epidermoid carcinoma on biopsy. The patient in her 75th year with arteriosclerotic heart disease was not considered a satisfactory candidate for pneumonectomy. In order to provide aeration of the lung promptly, 4 radon seeds for 3.6 millicuries were implanted in the tumor in the left main stem bronchus and the lung was re-expanded within a week as the tumor shrank and this was followed with 5000 r TD over an 8 cm spherical portal centered over the radon seeds. The patient lived four years and four months, died of other causes, namely a new fifth cancer, breast in origin and at autopsy no residual of the pulmonary neoplasm was found!

3. As an adjunct to external irradiation of squamous carcinoma of the trachea, four cases. In this situation where there is infiltration beyond the trachea itself and resection is not feasible, external irradiation has proved a useful tool and through the tracheostomy opening or by means of the bronchoscope, accurate transtracheal implantation can be achieved provided one is careful not to produce a severe esophagitis by overtreatment. There were in this group two excellent results with patients surviving six and three years and the latter still without evidence of re-activation.

4. The method is available as adjunct to implantation of radon seeds at open thoracotomy. There are six such cases in the group of 323 implanted at thoracotomy. There does not appear to have been any discernible aid to the patient by this method and such effect is presumably to be anticipated because usually when the chest is open and the lung available even though the extent of the tumor may preclude complete exposure of the tracheobronchial tree, accurate implantation about and even within the bronchus is feasible. Furthermore the combination of implants at thoracotomy and bronchoscopy fails to allow a differential opinion as to the value of this method. There have been three instances of polypoid epidermoid carcinoma within the tracheobronchial tree in this group of patients where at the end of the thoracotomy, bronchoscopic removal of as much of the endobronchial tumor as could safely be taken away has benefitted the patient by aiding aeration and drainage during the time before the radon implant could take its effect upon the tumor.

5. Endobronchial radon has been the sole treatment in three unusual cases. The first case is an 84 year old man with a carcinoma of the intrinsic larynx and simultaneous carcinoma in the left lower lobe bronchus. A laryngectomy was carried out and the endobronchial obstructive tumor was treated with a radon capsule for 1500 millicurie hours in four treatments. The patient lived over four years but in the last year of his life had recurrence of the obstructive phenomenon plus hemoptysis and presumably died from persistence of the endobronchial tumor. Unfortunately we did not have a chance to see him after the initial treatment. The second patient was a man of 54 with hemoptysis appearing some three years after a nephrectomy for primary kidney cancer. He was found to have a 6 mm polypoid lesion in the right bronchus intermedius which on biopsy proved to be metastatic renal cancer. It was treated at the site of the biopsy with 3 radon seeds at 1. millicurie each. There was no further hemoptysis and in the remaining 15 months of life no other evidence of endobronchial or pulmonary metastasis despite the fact that this

metastatic deposit seemed undoubtedly to have arisen in lymph channels beneath the mucosa of the bronchus. His death was due to involvement of thoracic and lumbar vertebrae with metastatic deposits from his kidney cancer. The third patient was a woman of 60 with hemoptysis, a shadow of atelectatis in the right middle lobe, and enlarged lymph nodes in the right supraclavicular area. Biopsies of the node and of the entrance to the right middle lobe showed reticulum cell lymphosarcoma. The lesion at the entrance to the right middle lobe was treated with 6 radon seeds at 1.6 millicurie each in two treatments seven days apart and the patient received 27 milligrams of nitrogen mustard intravenously in one dose. There was no other treatment and four years later there has been no other evidence of lymphosarcoma.

6. Endobronchial treatment may be helpful in partial control of the endobronchial and endotracheal element of adenomas. It is to be emphasized that this method is not in any way on a par with surgical extirpation of carcinoid or cylindromatous tumors which rather than being classified as "bronchial adenoma" are now being called, by most pathologists, low grade lung cancer. There are two such cases in this series. In one the patient was treated for 15 years by endobronchial radon implantation and cautery loop removal of that portion of the bronchial adenoma protruding into the right main stem bronchus. By these methods an open lumen was achieved during all this time though the patient had episodes of cough and hemoptysis and an occasional pulmonary infection. She had originally been denied surgery because of generalized arteriosclerosis with a hypertension ranging around 200/110. In the end arteriosclerotic intracranial changes led to her death. The bronchial adenoma was never completely brought under control but certainly obstruction of a major bronchus or serious hemorrhage was averted. The other patient in this group had a cylindromatous tumor of the trachea which was beyond the tracheal wall at the initial exploration. He lived for 13 years and though the cylindromatous disease spread down the trachea and into both main stem bronchi, airway was maintained with endobronchial treatments. His death was due to parenchymal pulmonary metastasis.

7. The use of this method has been most gratifying in treating recurrence of cancer in the bronchial stump following primary resection. There are ten such cases. In two instances the removed lung showed carcinoma in situ at the line of transsection at the main bronchus and these were both treated with capsule to the stump for 1200 millicurie hours. There were no deleterious effects in either instance

and one lived 15 months dying of distant metastasis without local recurrence and the other lived four years and four months and died of heart failure. The most satisfactory stump recurrence treatment was in a patient who had been a heavy smoker, had a left pneumonectomy for carcinoma within the left upper lobe bronchus of the epidermoid category and with the gross margin approximately 2 cm from the margin of bronchial transsection, who six years later had hemoptysis and biopsy proven recurrence in the left bronchial stump and was treated with 15.3 millicuries in radon seeds in three treatments over a month's period. There was a disagreeable esophagitis for four months but the patient is now living four years after the radon implantation and nine years after the pneumonectomy. It is our presumption that in these instances there is a true recurrence based somewhat on a study of 111 patients who had survived five years after resection for primary lung cancer. In 19 of these there then became manifest recurrence of cancer somewhere in the body but only one patient has shown a definite second lung cancer. In ten patients treated for stump recurrence none lived less than 18 months. Three are alive four, three and one-half and two years later. Survival time appears to be lengthened in this selected group though certainly statistical comparisons are not proper with such a small number of patients. It can be stated that lung cancer untreated will have, from the time of first appearance at the hospital, an average survival of six months whereas those implanted at thoracotomy have an average survival of 11 months and those resected of 13 months (including the postoperative deaths) whereas this selected group with endobronchial radon treatment has had an average survival of 29 months.

CONCLUSIONS

1. There are definite opportunities for the use of endobronchial isotopes principally in the form of radon seeds and capsules containing radon gas as an adjunct to treating primary or secondary cancer in the major air passages.

2. Local recurrences following pulmonary resection, primary epidermoid lesions of the trachea, and non-resectable adenomas are the most likely lesions to be improved by this treatment method.

3. It is recommended that marginal biopsies be secured for frozen section at the time of resection for primary or secondary lung cancer.

755 Park Ave.

Books Received

Broncoscopia. Principi di Diagnostica e Atlante de Fotografia Endoscopia

By *Luciano Cattaneo* and *Lucio di Guglielmo*, of the Otorhinological Clinic and the Institute of Radiology of the University of Padua. Cloth, 4to., 400 pages, handsomely illustrated in color and black-and-white. Rome, "Il Pensiero Scientifico" 1961. Price: L 15,000.

This atlas is so vividly and completely illustrated as to be highly instructive even to those who do not read Italian. Two chapers are devoted to anatomy, physiology and technique, the remaining seventeen to pulmonary diseases and foreign bodies. Completely documented.

Illustrations of the Nervous System. Atlas III

By *Louis Hausman, M.D.*, Professor of Clinical Medicine (Neurology) Emeritus, Cornell University Medical College, etc. Cloth, large 8vo., 168 pages, illustrated. Springfield, Charles C. Thomas, 1961. (Price $9.50)

A useful atlas of diagrammatic line drawings showing in great detail the complex innervation of the regions and organs of the body, often so difficult of demonstration.

Fortschritte der Kiefer- und Gesichts-Chirurgie (Advances in Maxillary and Facial Surgery)

A comprehensive collection of articles by some forty contributors, edited by *Prof. Dr. Karl Schuchardt*, Director of the University Polyclinic for Dental, Oral and Maxillary Diseases, Eppendorf. Cloth, large 8vo., 352 pages, illustrated. Stuttgart, Georg Thieme Verlag, 1960. (Intercontinental Book Corporation, N.Y. 16, N.Y.) (Price $27.60) In German.

This is Vol. VI of a yearbook, comprising the scientific papers of a conference of the Deutsche Gesellschaft für Kiefer- und Gesichtschirurgie (German Society for Maxillary and Facial Surgery), held at Düsseldorf in July 1959.

Common Diseases of the Ear, Nose and Throat (3d Edition)

By *Philip Reading, M.S.(Lond.), F.R.C.S.(Eng.)*, Surgeon to Ear and Throat Department, Guy's Hospital, London. Cloth, 8vo., 264 pages, illustrated. Boston, Little, Brown and Co., 1961. (Price $8.00)

The A, B, C's of otolaryngology. Strictly for "the newly qualified practitioner" but rather more informative than most of these little books.

JULIAN B. COHN

1892 - 1961

On July 9, 1961, Julian B. Cohn, for thirty-seven years Manager of the Annals Publishing Company, died suddenly at Vienna while en route to Paris to attend the International Congress of Otorhinolaryngology.

Mr. Cohn assumed the active business management of the ANNALS in 1924, when ownership was acquired by his father-in-law, Dr. Hanau W. Loeb, who had been editor virtually since the beginning in 1892. His warm interest and constant, unobtrusive co-operation with the editorial department, the printers, in fact with all of the sundry personnel, maintained a spirit of harmony unruffled by stresses and irritations.

His widow, Irene Loeb Cohn, will continue in his place as head of the publication which has always been a protegé of the family, whose sentimental care has contributed to a tradition of good taste and high standards.

Until recently Mr. Cohn had been President and Chairman of the Board of the Weil Clothing Company. A leader in many social and charitable movements he was, among other activities, for some years Vice-Chairman of the Social Planning Council of St. Louis and St. Louis County and Chairman of the St. Louis County Family Service Agency. During the depression of 1929 he headed the Committee of One Hundred, composed of representatives of one hundred charitable and religious organizations, whose assistance to the State Legislature rendered great service in alleviating the distress of the unemployed. At the time of his death he was a regional adviser to the Small Business Administration.

Mr. Cohn is survived by his widow, two daughters and six grandchildren.

JULIAN B. COHN

Abstracts of Current Articles

EAR

Mozart's External Ear

Kerner, D.: Z. Laryng. 40:475-478, 1961.

This is a report on a historical curiosity. W. A. Mozart as shown in most pictures carried his hair long over the sides of his head. He apparently did so in order to cover his congenitally misshapen ears. According to a drawing by his youngest son, there were no tragus and antitragus, the earlobe was missing, and the entrance to the external canal was reduced to a narrow slit. This is the more remarkable as this external malformation was apparently associated with an extremely well-functioning inner ear and central auditory system. There are many stories on record which vouch for Mozart's keen sense of hearing, for example his writing down from memory an entire mass he had just heard, the score of which had never been made available to the public.

TONNDORF

Reversed-Ear Syndrome and the Mechanism of Barotrauma

Jarrett, A.: Brit. M. J. 2:483-486 (Aug. 19) 1961.

"Reversed ear" is a term used by divers to describe what they felt was an outward bulging and rupture of the tympanic membrane. Lt. Jarrett examined 14 such cases, an incidence of 0.5% of all dives made during the 4 month interval. Nine of the 14 had no symptoms during the dive, and 5 stated they had temporary difficulty clearing the ears in descent. All presented with blood on the pinna. After cleaning the ear with hydrogen peroxide, the drumhead in each case was found to be intact and freely movable. The meatus contained subcutaneous petechiae, which may have progressed to blood-filled blisters, which on rupturing oozed, leaving ragged curtains of skin. Treatment consisted of cessation of diving, local use of hydrogen peroxide, and prophylactic sulphadimidine. There were no infections, and all but one healed within two weeks.

The common flexible rubber suit and hood worn develops a negative pressure, demonstrated by the author to be −659 mm Hg at 80 ft. This, combined with increased body and blood-pressure in diving, passively dilates the vessels on the surface which may rupture. Similar effects of barotrauma are found when goggles cover the eyes only, causing conjunctival hemorrhage, and in the hemoptysis sometimes occurring in those who dive without breathing apparatus.

Using a pressure-sealed Siegle's speculum in a subject's ear, Jarrett reproduced the red petechiae in the canal at only 120 mm Hg; and, at 150 mm Hg negative pressure, petechiae coalesced to form a hemorrhagic bulla in another patient. In both cases the tympanic membrane returned to normal when the pressure was released but the canal changes remained. He recommends only porous ear covering, avoiding pressure differences.

TRIBLE

Treatment of the Mastoid Cells in Tympanoplasty

Goto, T.: J. of the Oto-Rhino-Laryngologic Soc. of Japan 64:1011-1016, 1961.

The author states that in tympanoplasty for simple, noncomplicated chronic mastoiditis, the mastoid cells should not be exenterated. The reactions of the tympanum, the ossicles and the mastoid cells in chronic mastoiditis present different histologic pictures. The author demonstrated phagocytic process of the epithelium of chronically infected mastoid cells. He considers the process being a progressive healing process. This can be hastened by judicious use of antibiotics. In most cases, otorrhea in acute exacerbation of chronic otitis media is limited to the tympanic cavity, including the attic, but seldom observed in the mastoid cells. Granulations around the ossicles develop obstruction in the aditus. Thus, the mastoid cells are isolated from the tympanum in its suppurative process. Goto states that the postoperative epithelization of the mastoid cavity is achieved with much difficulty. Within a few months after the tympanoplasty, there is a great tendency for the formation of granulation tissue. The dermal transplants tend to form cysts in some cases. In others, the epithelium atrophies and denudation of the bony bed occurs. Goto attributes this undesirable result to 1) dermatitis due to failure in maintaining meticulous cleanliness of the cavity, 2) formation of cholesteatoma, 3) failure to attain complete exenteration of cellular structures when pneumatization is extensive, 4) poor host site for the transplant to thrive. The author does not believe that the use of pulverized bone is the answer to filling a large operative cavity. Like Wülstein, he believes

that the attic and aditus should be thoroughly inspected through the fenestra and the required treatments be given according to their indications.

HARA-TSUGAWA

New Aspects in Employing Transitory Phenomena for the Differential Diagnosis of Perceptive Deafness

Lucas, A.: J. Laryng. 40:521-531, 1961.

After discussing various audiometric methods for supra-threshold testing, the author describes briefly the principle of a new audiometer he designed with L. Pimonow which he calls an impuls-audiometer. This instrument permits production of electrical transients of any desired form by means of a neon bulb-photocell arrangement with a slotted disk rotating between the two. The form of the slots and the rotating speed of the disk determine the shape and duration of the transients. Although an impressively long bibliography is appended to the paper referring to the pertinent clinical, audiological, and auditory-physiological literature, the reviewer missed references to basic technical papers such as those by D. Gabor and J. F. Schouten, among others. Without giving tangible evidence, the author claims that this new audiometer will make speech audiometry "practically" obsolete. Curiously, the latter statement appears only in the German and French summaries of the paper (author is French), but not in the English version which at this point reads: ". . . the investigations are valuable in the cerebral diagnosis of the interpretation of speech."

This reviewer has the uncomfortable feeling that this may be another in a series of sensational French papers which have attained more publicity than they deserve. This is to be regretted in view of the many fine contributions made by other French scientists.

TONNDORF

Electric Trauma in Otology

Kittel, G.: Zschr. Laryng. 40:684-693, 1961.

Three cases of electric trauma (lightning, high-voltage wire) are presented. In two of these the accident had occurred 10 years, in the third 2 years, prior to the report. There were no indications of concomitant head injuries, due to falling from a ladder for instance. In the case caused by lightning, the possibility of an initial acoustic trauma cannot be excluded with certainty. (There are reports to

that effect in the literature.) However, the present audiological examination of all three cases indicated retrolabyrinthine or central types of hearing impairment. Vestibular aberrations were also present. Subjectively, even in the 10-year cases, there were dizziness and occipital headaches, but also specfic neurological signs such as intermittent sensory aphasia in one case and anosmia in another.

After discussing the relevant literature (there were only scattered reports on single cases), the author comes to the conclusion that in pure electric trauma (i.e. without concomitant head injury or acoustic trauma) the site of the lesion is either predominantly central or in the VIII nerve. Cochlear degeneration has been seen occasionally and also, usually as an initial transient phenomenon, what appears to be a labyrinthine hydrops. The acoustic trauma associated with lightning may lead to rupture of the eardrum and other forms of middle-ear injuries.

TONNDORF

Clinical Findings in Barotrauma of the Cochlea (Les Barotraumatismes Cochleaires. Donnees Cliniques)

Appaix, A., Grinda, M., Hennin J. et *Nourrit,* P. (Marseille): Ann. Oto-Laryng. (Paris) 78:6:359-71 (June) 1961.

The authors have examined many patients involved in underwater diving—such as workmen of naval shipyards or sportsmen in southern France. Twenty-five cases of nerve deafness were observed among these patients; 10 of them were acute cases. The study of the 10 acute cases revealed that all of them were trained men in underwater diving without previous history of Caisson disease and no history of ear-nose-and-throat problems prior to or immediately before the accident. The average depth reached during the dive was between 30 and 60 feet and the average age of the divers was 30 years.. The following auricular manifestations were present at surfacing in these 10 cases: unilateral blocked ear, tinnitus, unilateral deafness, occasional vertigo and severe unilateral otalgia in 4 cases. The study of the 15 chronic cases showed a gradual loss of hearing throughout the years among trained underwater divers practicing the profession in an average of 15 years. Three of them had a history of previous caisson disease; the audiogram showed a loss in the high and middle frequencies associated with positive recruitement in 60%. The authors describe their treatment. Immediate recompression is the only effective treatment which was performed on 3 patients with 100% result.

BALLA

Cochlear Microphonics and Autonomic Nervous System

Watanabe, Y.: J. of Oto-rhino-laryng. Soc. of Japan 64:1325 (Aug.) 1961.

The changes in cochlear microphonics (CM) in relation to the various stimulations to the autonomic nervous system were studied on guinea pigs.

1. Injection of Atropin (0.5 mg) or Acetylcholine (100 mg) into the abdominal cavity resulted in reduction of CM, but Pilocarpin (10 mg) or Adrenalin (1 mg) failed to produce consistent changes in CM.

2. Application of 10% Nicotine to the superior cervical ganglion caused initial reduction of CM within 10 seconds, and then CM increased for the next 25 minutes.

3. Excision of the cervical sympathetic nerve or ganglion increased CM at the beginning followed by gradual reduction.

4. Excision of the vagus nerve had little influence on CM in some cases, but slightly reduced CM were observed in the others.

5. Electric stimulation (40 cps, 0.5-5 v, 30 sec) on the sympathetic nerve or ganglion reduced CM for only 10 to 50 seconds, then CM recovered to the normal in most cases.

6. Electric stimulation of the vagus nerve brought no changes in CM.

HARA-TSUGAWA

NOSE

Radium Irradiation for Treatment of Hyperplastic Nasal Mucous Membrane

Takenaka, B., Yokoi, K., and Ogino, F.: Otolaryngology (Tokyo) 33:479-484, 1961.

Takenaka and his associates applied 1.5 mm x 15 mm radium tube wrapped in cotton to the hyperplastic nasal mucosa, placing it above the lower turbinate and below the middle turbinate. Each received 10 mg-1 hour per week with the total amount ranging from 50-70 mg. One month to 3 years previous to radium irradiation the hyperplastic nasal mucosa had been removed. Following the radiation therapy subjectively there was reduced nasal discharge and lessened sense of nasal obstruction in varying degrees.

Histologic study indicated there was a marked reduction in infiltration of round cells, eosinophiles and lymphocytes. The mucous glands appeared vacuolated. With this technique the authors felt that nasal mucosa regained its normal function and the patients were made relatively symptom-free. There were no ill side-effects.

HARA

THROAT

Reestablishment of Swallowing in Bulbar and Hemibulbar Paralysis (Réestablissement de la déglutition dans les cas de paralysie bulbaire et hémibulbaire)

Réthi Aurél (Budapest) Ann. Oto-Laryng. (Paris) 78:6:372-77 (June) 1961.

The author briefly discusses the pathologic manifestations involving the laryngo-pharynx in bulbar and hemibulbar paralysis, paying special attention to repeated attacks of aspiration pneumonia. He describes a surgical procedure in detail with illustrations for the correction of the above problem and presents one successful case. The purpose of the operation is to stricture the dilated, atonic hemipharynx, preventing the accumulation of food and saliva in a dilated pocket. Vertical incision is carried out alongside the anterior border of the sternomastoid, the thyroid cartilage is exposed and the inferior constrictor of the pharynx is transsected alongside the posterior border of the thyroid cartilage. The dilated pharyngeal mucosal wall is exposed, without entering the pharynx, and sutured in such a fashion that it creates a tight hemipharynx.

BALLA

MISCELLANEOUS

Carotid Pain

Martorell, F.: Acta O.R.L. Ibero-Americana XLL, 2:116-120, 1961.

The author discusses the syndrome of "carotid pain" described by Hilger in 1949. He describes the multiple sites of edema in a patient whose various crises were always accompanied by a sudden tenderness and swelling over the bifurcation of the left carotid. The first episode involved the pharynx, causing pain and difficulty in

swallowing. A tonsillectomy was performed. Subsequently a sinusitis was suspected; later a phlegmon of the tongue, and on another occasion edema of the larynx. Suspected teeth were extracted. The correct diagnosis was made after a detachment of the retina due to edema which resulted following a disturbance of the carotid artery. Injections of gynergen quickly controlled subsequent attacks. The author stresses the importance of recognizing that the syndrome may have many different manifestations depending on which branch of the external carotid is involved. The syndrome is similar to migraine, with a cervical-facial distribution instead of cranial. Like all other vascular disturbances it is considered to be due to an autonomic system inbalance brought about by emotional, allergic, or inherited factors.

ALFARO

Two Cases of Foreign Body Entering the Inferior Respiratory System Through the Skin (Deux cas de corps etrangers des conduits respiratoires inferieurs introduits par la voie transcutanée)

Femenic, B., Milojevic, B., et *Pasini, C.*: Les Annales D'oto-laryngologie 78:3:134-137, 1961.

The authors present two cases of foreign bodies introduced into the respiratory system, by accident through the skin.

The first case posed a diagnostic problem because of repeated pulmonary infections. A piece of wood accidentally pierced the parenchyma of the lung through the skin of the thorax. Finally, it was discovered and removed by bronchoscopy.

In the second case, a foreign body entering through the skin of the neck was seen in the pyriform sinus and removed.

The authors stress the importance of endoscopy in the diagnosis of infections of the respiratory system.

GOZUM

Statistical Study on Cervical Resections for the Control of Malignant Tumors

Nakamura, F., and Associates: Otolaryngology Tokyo 33:397-401 (May) 1961.

Nakamura and his co-workers recorded their observations in dealing with 164 cases of malignant tumors of the head and neck in

a 6-year period. Follow-up study was conducted in 130. These tumors and their distribution were as follows:

1. Nasopharyngeal	9
2. Paranasal sinuses	43
3. Tongue	21
4. Tonsils	14
5. Pharynx	10
6. Larynx	54
7. Cervical esophagus	13

There were 111 males and 53 females. Sarcoma was limited to the tonsils. Squamous type tumors were found in all other areas.

Of the nine cases of nasopharyngeal tumors, eight had cervical metastasis. In 35% of tumors originating in the sinuses, in 40 to 60% of those involving the tongue, and in 44% of those invading the larynx, cervical metastasis was present at the time of the primary operation.

The authors concluded that beneficial results were obtained by neck resection in cancers of the larynx, tongue and oral cavity; whereas, with cancers occurring in the paranasal and nasopharyngeal cavities, until the primary lesion is completely removed, neck dissection is not equally helpful.

HARA

Statistical Data in Connection with 131 Malignant Tumors of the Ethmoido-maxillary area (Elements statistiques a propos de 131 tumeurs malignes du massif ethmoido-maxillaire)

Bourguet, J., Le Branchu, J., Limbour, J. et *Chesnais, J.*: Les Annales d'Otolaryngologie 78:7-8:464-473, 1961

In this presentation the authors give the statistical data on 131 malignant tumors seen during the last fourteen years. The youngest patient was three months old and the oldest 80 years. The largest number of cases were found in the sixth decade. Seventy per cent occurred during the fourth to the seventh decades. The authors observed that carcinoma in adults occurred eight times more often than sarcoma. Sarcoma and carcinoma occurred at the same rate in chil-

dren. Treatment consisted of surgery, radium application, and x-ray therapy. The survival rate was rather low; 62.2% of the patients lived one year, 28.8% three years, 15.3% five years, and only 4.8% ten years.

GOZUM

Comprehensive Resection of the Cancer Bearing Upper Jaw

Fujimori, N.: J. of ORL Soc'y of Japan 64:1260- (Aug.) 1961.

Fujimori reports a five-year survival rate of 40% among 35 patients who were seen at Keio University Hospital. These patients were subjected to a radical one block excision of the tumor with a wide margin of healthy tissue. The operation was performed under general anesthesia administered through the previously prepared tracheotomy stoma. The procedure included the removal of the maxilla, the muscles of mastication with temporal muscles and the orbital contents without splitting the upper jaw. This block contains the greater part of the roof of the frontal sinus, ethmoidal and sphenoid sinuses and the orbit, and the median wall of the temporal fossa. These structures form the base of the skull, exposing the dura. To prevent postoperative meningismus and meningitis, an incision is made in the meninges to induce a copious flow of the cerebrospinal fluid. An adequate amount of antibiotics si given 48-72 hours before and after surgery. Some receive preoperative whole blood transfusion. In others, blood loss is controlled by transfusion either during or following the operation. Preoperatively, artificial dentures are made to fill the palatine defect.

Within three months following surgery, 22 died due to suppurative meningitis, septicemia, cardiac failures, tracheal obstruction, pulmonary invasion and other, unrelated, conditions. Histological examination showed epidermoid carcinoma (31), carcinoma simplex (2), adenocarcinoma (1), and small cell carcinoma (1). Both the patients and their immediate relatives are emotionally prepared in anticipation of the facial deformity following the surgery. The tracheal stoma is closed in a week. Oral feeding commences usually at the same time. Postoperative irradiation of 6000 R is given in 3-4 weeks.

HARA-TSUGAWA

Notices

AMERICAN BOARD OF OTOLARYNGOLOGY

The American Board of Otolaryngology will conduct only one examination in 1962, and this will be held at the Palmer House in Chicago, Illinois, October 28th - November 1st.

ROYAL SOCIETY OF MEDICINE

Members of the American Laryngological Association, the American Otological Society, and the American "Triological" Society who will be in the United Kingdom at the time of any of the meetings of the Royal Society of Medicine, Sections on Laryngology and Otology, will be very welcome. Meetings are scheduled for Feb. 2, March 2, May 4, and the Summer Meeting at Canterbury June 29 and 30, 1962.

UNIVERSITY OF MINNESOTA

The Center for Continuation Study, University of Minnesota, Minneapolis, Minnesota, will present a course in Otolaryngology for Specialists on January 25-27, 1962.

UNIVERSITY OF ILLINOIS

The Department of Otolaryngology, University of Illinois College of Medicine, will conduct a postgraduate course in Laryngology and Bronchoesophagology from April 2 through 14, 1962, under the

direction of Paul H. Holinger, M.D. Registration will be limited to fifteen physicians.

Interested registrants will please write the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

SIXTH INTERNATIONAL CONGRESS OF AUDIOLOGY

The sixth International Congress of Audiology will be held in Leyden, The Netherlands, from September 5 to 8, 1962. The president is Prof. Dr. H.A.E. van Dishoeck, and the secretary Dr. A. Spoor.

Three round-table talks are planned, with associated and free papers. The subject of the round tables are: "Frequency Analysis of the Normal and Pathological Ear." Moderator: Prof. Dr. G. von Békésy; "Central Deafness in Children," Moderator: Prof. Dr. J. M. Tato; "Psychogenic Deafness and Simulation," Moderator: Prof. Dr. H.A.E. van Dishoeck.

Official languages of the Congress are English, French, German and Spanish. Working languages will be English and French.

The address of the secretariat is: Ear-Nose-Throat Department, Academisch Ziekenhuis, Leiden (The Netherlands).

UNIVERSITY OF TEXAS

The Post Graduate School of the University of Texas and the Baylor University College of Medicine will present a course in allergy to be conducted by Herbert J. Rinkel, M.D., February 5th through February 9th, 1962, in Houston, Texas.

The course will be followed by a meeting of the Gulf Coast Allergy Study Group, February 9th and 10th.

For further information, write: Office of the Dean, University of Texas Post Graduate School of Medicine, 410 Jesse Jones Library Building, Houston 25, Texas.

PAN-PACIFIC SURGICAL ASSOCIATION

The Otolaryngology Section of the Ninth Congress of the Pan-Pacific Surgical Association will be held November 5-13, 1963 in Honolulu, Hawaii.

PAN-PACIFIC LECTURE SEMINAR

The First Pan-Pacific Mobile Educational Lecture Seminar will be held November 13 to December 10, 1963, in New Zealand, Australia, Thailand, the Philippines, Hong Kong and Japan.

All Otolaryngologists are cardially invited to attend both of these meetings. The Ninth Congress offers an extensive otolaryngological program with leading international otolaryngologists participating.

The Seminar through the Pacific area offers, for the first time, scientific meetings in each country presenting medical material unique to the areas.

For further information, please write Dr. F. J. Pinkerton, Director General, Pan-Pacific Surgical Association, Suite 570, Alexander Young Building, Honolulu 13, Hawaii.

THE AMERICAN COLLEGE OF ALLERGISTS

The American College of Allergists will present a Graduate Instructional Course at their Eighteenth Annual Congress, April 1 - 6, 1962, Hotel Radisson, Minneapolis, Minnesota. For further information, write to: John D. Gillaspie, M.D., Treasurer, 2141 14th Street, Boulder, Colorado.

HANSEL FOUNDATION COURSE

A Hansel Foundation course is planned to cover subjects in medical otolaryngology, such as the diagnosis and treatment of vascular headaches, Menière's Syndrome, and related phenomena, effective use of bacterial and viral vaccines, use of antibiotics and other drugs, aerosol therapy and other subjects with special reference to allergy

and immunity. The course will be given May 28th through June 1st, 1962, at the Diplomat Motel in St. Louis. Further information may be obtained from the Director: French K. Hansel, M.D., 634 North Grand Ave., St. Louis 3, Mo.

THE MOUNT SINAI HOSPITAL

An intensive postgraduate course in Rhinoplasty, Reconstructive Surgery of the Nasal Septum and Otoplasty will be given January 13, 1962, to January 26, 1962, by Dr. Irving B. Goldman and staff at the Mount Sinai Hospital, New York, in affiliation with Columbia University.

Candidates should apply to Registrar for Postgraduate Medical Instruction, Mount Sinai Hospital, Fifth Avenue and 100th Street, New York 29, N.Y.

OFFICERS

OF THE

NATIONAL AND INTERNATIONAL OTOLARYNGOLOGICAL SOCIETIES

American Academy of Ophthalmology and Otolaryngology

President: John H. Dunnington, M.D., New York
Executive Secretary: Dr. William L. Benedict, Mayo Clinic, Rochester, Minn.

American Board of Otolaryngology

President: Bernard J. McMahon, M.D., St. Louis
Secretary: Dean M. Lierle, M.D., University Hospital, Iowa City, Iowa

American Broncho-Esophagological Association

President: Alden H. Miller, M.D., Los Angeles, Calif.
Secretary: Daniel C. Baker, Jr., M.D., 903 Park Ave., New York 21, N. Y.
Meeting: Sheraton-Dallas Hotel, Dallas, Tex., May 1-2, 1962

American Laryngological Association

President: Dean M. Lierle, M.D.
Secretary: Lyman A. Richards, M.D., 12 Clovelly Rd., Wellesley Hills 81, Mass.
Meeting: Sheraton-Dallas Hotel, Dallas, Tex., May 4-5, 1962

American Laryngological, Rhinological and Otological Society, Inc.

President: John R. Lindsay, M.D., Chicago
Secretary: C. Stewart Nash, M.D., 708 Medical Arts Bldg., Rochester, N.Y.
Meeting: Sheraton-Dallas Hotel, Dallas, Tex., May 1-3, 1962

American Medical Association, Section on Laryngology, Otology and Rhinology

Chairman: Howard P. House, M.D.
Secretary: Walter E. Heck, M.D., 3905 Sacramento St., San Francisco 18, Cal.
Meeting: Chicago, June 24-28, 1962 (revised date)

American Otological Society

President: Lawrence R. Boies, M.D.
Secretary: James A. Moore, M.D., 526 E. 66th Street, New York 21, N. Y.
Meeting: Sheraton-Dallas Hotel, Dallas, Tex., April 29-30, 1962

Society of Military Otolaryngologists

President: Aubrey K. Brown, Lt. Col. USA MC

Secretary-Treasurer: Donald J. Joseph, Lt. Col. USA MC, Madigan General Hospital, Tacoma, Washington

International Bronchoesophagological Society

President: Paul H. Holinger, M.D.

Secretary: Charles M. Norris, M.D., 3401 N. Broad Street, Philadelphia 40, Pa.

Meeting: 1963

Pan-American Association of Oto-Rhino-Laryngology and Broncho-Esophagology

President: Dr. Plinio de Mattos Barretto, São Paulo, Brazil

Acting Executive Secretary: Dr. Charles M. Norris, 3401 N. Broad St., Philadelphia 40, Pennsylvania

Meeting: Eighth Pan-American Congress of Oto-Rhino-Laryngology and Broncho-Esophagology; President: Dr. Alfredo Celis Pérez, Valencia, Venezuela; February, 1962, Venezuela

Pacific Coast Oto-Ophthalmological Society

President: Clarence W. Trexler, M.D.

Secretary-Treasurer: Alden H. Miller, M.D., 500 S. Lucus Ave., Los Angeles, Calif.

Canadian Otolaryngological Society

President: Dr. Walter Alexander

Secretary: Dr. Kenneth McAskile, 174 St. George Street, Toronto 5, Ontario

Meeting: Royal Alexandra Hotel, Winnipeg, Manitoba, June 25-27, 1962

Mexican Society of Otolaryngology

President: Dr. Rafael Giorgana

Secretary: Dr. Carlos Valenzuela, Monterrey 47 Mexico 7, D.F.

Royal Society of Medicine

Section of Laryngology

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